

**RADIUM TREATMENT OF
CANCER**

**RECENT ADVANCES IN
SURGERY**

By W H OGILVIE, M D, F R C S,
Assistant Surgeon, Guy's Hospital
108 Illustrations 15s.

**THE OPERATIONS OF
SURGERY**

By R P ROWLANDS, M S, F R C S,
and PHILIP TURNER, M S, F R C S
Surgeons, Guy's Hospital Seventh
Edition 2 Volumes 995 Illustra-
tions, some in colour 70s

**MINOR SURGERY AND
BANDAGING**

By GWYNNE WILLIAMS, M S,
F R C S, Surgeon, University College
Hospital Nineteenth Edition 217
Illustrations 10s 6d

SURGICAL ANATOMY

By GRANT MASSIE, M B, M S,
F R C S, Senior Demonstrator of
Anatomy and Surgical Tutor, Guy's
Hospital 121 Illustrations, some in
colour 15s

SURGERY IN THE TROPICS

By Sir FRANK P CONNOR, D S O,
F R C S, D I M & H, Professor of
Surgery, Bengal Medical College 99
Illustrations 12s 6d

J & A CHURCHILL

RADIUM TREATMENT OF CANCER

BY
STANFORD CADE,
F R C S (Eng.)

*Assistant Surgeon Joint Lecturer on Surgery
and Teacher of Practical Surgery Westminster
Hospital Late Hunterian Professor and President
Cade Lecturer Royal College of Surgeons of
England*

WITH 13 COLOURED PLATES AND
49 TEXT FIGURES



LONDON
J & A CHURCHILL
40 CLOUDESTER PLACE
PORTMAN SQUARE
1929

FOREWORD

THE book to which we have the pleasure of contributing this foreword is the exclusive personal work of Mr Stanford Cade

Since the use of radium began at Westminster nearly five years ago, there has been free interchange of experience, active pooling of ideas, and mutual adoption of suggestions, so that, to-day, it is difficult to be sure which amongst us contributed any particular point of technique that has been added to our original plans based on the procedures of the Paris and Brussels Schools

At the same time, Mr Stanford Cade has treated more cases than any other individual member of the staff, whilst his enthusiasm, intense application and standardisation of method have been an inspiration to us all. We have had every opportunity of seeing his patients, the failures as well as the successes

The following pages embody the actual work with which we are all familiar. All of it has been practised also by some one or more of us, some of it by all, and we trust the publication of the little volume will prove as valuable a help to many readers as his example and co-operation have proved to

THE AUTHOR'S COLLEAGUES on the Staff of the WESTMINSTER HOSPITAL

William Turner	A Tudor Edwards
Arthur Evans	G T Mullaly
E Rock Carling	Gilbert Chubb
Stanley Dodd	Aubrey Goodwin
C Price Thomas	

AUTHOR'S PREFACE

IN presenting this book to the medical public I do not wish to appear a partisan of a certain method of treatment of cancer. I am primarily a surgeon, and radium therapy is only an effective weapon in the armamentarium available for the treatment of the patient afflicted with cancer. Patients are entitled to expect the selection and use of the most effective form of treatment for their special needs. If the choice of treatment in a given case of cancer depends upon a surgeon not conversant with the possibilities of radium, the choice will inevitably be that of surgery; the converse is true and is applicable to the radiologist. Radium needs a surgery of access and surgery needs radium if the best is to be given to the patient. Radium treatment of cancer is in its infancy, it demands special knowledge, and in those who are using it an aptitude to adapt themselves to new lines of thought and new methods of technique. The methods described in these pages are the methods of to-day, and in a science so young and of so rapid development they may be of historical interest only before many years or even months have passed.

Before long chemistry and photo-therapy may become inseparable adjuncts of radium surgery.

I have tried to illustrate the technique applicable in various anatomical situations and some of the results obtained by quoting selected cases. A complete documentation will be found in the forthcoming volume of the Westminster Hospital Reports (volume 20). Statistical data are excluded as their value at present is of little importance, sufficient time not having elapsed to compare results with those of purely surgical methods. The majority of the work was done at Westminster Hospital; it has been done by all the members of the surgical staff, and it is significant that even at this early stage, about five years

after the first radium treatment, certain types of cancer, such as that of the tongue, are only exceptionally treated by diathermy excision, and then only to relieve the patient from the intolerable presence of a mass of malignant tissue filling the oral cavity. The advent of radium therapy is not the end of surgery, as some enthusiasts have declared after a few brief months' acquaintance with radium. It is, on the contrary, the beginning of a new era of surgery—less destructive and with wider scope than ever before. No preface to a book on radium therapy can be complete without a reference to the two great schools—the Fondation Curie of Paris and the Radium Institute of Brussels. It is with a sense of gratitude that I record my admiration for Professor Regaud and his collaborators, Lacassagne, Monod, Coutard, Hautant and Roux-Berger of the former, and to Professor Bayet and Drs. Sluys, Neuman, Delporte, Cahen and Ledoux of the latter.

I am indebted to them as pioneers of modern radium therapy on scientific lines, for their hospitality and for the free use I have made of their teaching and publications.

To my colleagues at Westminster Hospital I wish to express my gratitude for their co-operation in the development of the radium department of the hospital, and for many hints and suggestions which are the essence of a united effort to obtain better results. Mr. Arthur Evans has been most generous in placing at my disposal for long periods of time beds occupied by cancer patients, his co-operation in the clinical work has been invaluable and his help a constant encouragement. To Mr. Rock Carling I am indebted for his criticism of the methods and for the work in connection with this manuscript. To Dr. H. T. Flint for revising the section on the physics of radium, to Drs. Braxton Hicks and F. H. M. Hocking for the laboratory work in connection with the pathology and bio-chemistry of cancer, and to Mr. A. Clarkson for the preparation of dental appliances.

Finally, I wish to offer my thanks to Mr. Douglas Harmer for the criticism of the section on laryngeal cancer and for

all I have had the privilege of learning from him, and to Sir Charles Gordon-Watson for reading the chapter on Cancer of the Rectum, for placing at my disposal notes of some of his cases and for the loan of a drawing.

Westminster Hospital possesses now a considerable quantity of radium, purchased from funds given by the public for the purpose—the fund has grown around original gifts of Mr. Austin Taylor and the Prudential Assurance Company—and this made it possible for the staff to develop the technique of radium therapy. The Radium Institute, London, has been generous in supplying me with radon seeds and affording me facilities to work there, although their beds are few and their waiting-list long. I wish to thank Mr. Hayward Pinch for the facilities afforded to me and Drs. Philip Gosse and Roy Ward for their welcome and friendly help. I am indebted to Dr. Coldwell for the radiograms, to Mr. Sewell for all the coloured drawings, to Mr. Francis Rock Carling for the diagrams, and to Mr. Amyas McKenzie for the photographs.

STANFORD CADE

86, HAVILLY STREET,
W 1

CONTENTS

	PAGE
Foreword	v
Author's Preface	vi
List of Coloured Plates	v
Introduction	i
CHAPTER	
I Radioactivity	3
II Methods of Irradiation	9
III General Principles of Radium Therapy	19
IV Tongue and Buccal Cavity	28
V Cervical Lymphatic Glands	54
VI Pharynx and Larynx	66
VII Breast	74
VIII Rectum	86
IX Prostate Bladder, Penis Urethra Vulva Vagina	101
X Uterus	115
XI Oesophagus and Stomach	123
XII Lungs	132
XIII Central Nervous System	157
XIV Skin	147
XV Sarcoma	150
XVI Protection of Radium Workers	154
Index	155

LIST OF COLOURED PLATES

PLATE		TO PAGE
I	Epithelioma of Tongue, Papilliferous Type	28
II	„ „ Ulcerative Type	32
III	„ Floor of Mouth	38
IV	„ Tongue, Ulcerative and Nodular Type	44
V	„ Palate, Cauliflower Type	46
VI	„ Tonsil and Uvula, Ulcerative Type	48
VII	„ Lip—Nodular Type	52
VIII	„ „ Ulcerative Type	54
IX	Peeling after Radium Collar	64
X	Epithelioma of Penis	106
XI	Malignant Inguinal Gland	108
XII	The same as Plate XI after treatment	110
XIII	Epithelioma of Skin, Anterior Part of Thigh	148

RADIUM TREATMENT OF CANCER

INTRODUCTION

UNTIL recently the principle underlying the treatment of cancer was the elimination of the growth by excision with knife or diathermy. The vital question for each individual case was 'Is it removable?' The answer varied with the site of the growth, the skill and courage of the surgeon, the general condition of the patient and the presence of recognisable metastasis. Even in its widest sense the measure of operability depended on the question "Is the lesion removable?" and not on the question "Is the removal of the lesion going to cure the patient?" In the last ten years rapid progress of radium therapy has changed the conception of operability, and for the disappearance of the cancerous lesion it is no longer imperative to rely entirely upon the scalpel. What has radium added to the older methods of treatment? No one claims it as a specific for malignant disease. It has a limited use, but wider than that of surgery alone. In certain situations it has displaced the knife. In others it has added to it a possible means of prolonging life. One fact stands out very clearly: no patient, however "inoperable," should remain untreated. With the experiences of the Radium Institutes of Paris and Brussels as a starting point, Westminster Hospital has, for the last five years, treated a sufficient number of patients to justify the publication of this volume. No permanency of results is claimed, and the frequent changes of technique are signs of continuous progress. The possibilities of radium treatment are appre-

ciated by all the surgeons of Westminster Hospital to such an extent that it has become a daily routine, and some forms of cancer such as tongue, lip, palate and brain are now entirely treated by radium. We feel confident that in a few years' time the same will be said about cancer of the breast and uterus. The treatment of cancer by radium relies upon the selective action of radium on malignant cells. This selective action is due to the greater sensitivity of malignant cells to irradiation as compared to normal cells.

The combination of the biological factor of selectivity with the power of penetration of γ rays gives the possibility of treating lesions which are irremovable either because of their situation or because of the involvement of important structures. Further, radium therapy abolishes or at least minimises, operative mortality and mutilation. It enlarges the field of "treatable" cases beyond the limits imposed on purely operative surgery.

CHAPTER I

RADIOACTIVITY

RADIUM belongs to the group of radioactive elements. Radioactivity is defined as the spontaneous disintegration of an element, in the process of which the atomic nucleus ejects helium nuclei or single negative particles or both together. In many cases the process is accompanied by the emission of radiation. The three products referred to are described by Rutherford as α , β and γ rays. Radioactive bodies are thus a spontaneous source of energy, a fraction of which is localised in these rays.

α RAYS

α rays consist of helium atoms positively charged, they are given off at a velocity of 18,000 miles per second. One mgm of radium gives off each second 136 millions helium particles. They represent about 92 per cent of the total energy of radioactive bodies. Their penetrating power is very small and they are absorbed by a few centimetres of air, by such thin screens as a sheet of ordinary writing paper and by 0.06 mm of aluminium. α rays have a very intense ionising power and a single α particle from radium has been found to produce over 100,000 ions in a range of 3.30 cm in air.

β RAYS

β rays are analogous to the cathode rays, they consist of single negative electrons given off at a velocity varying from 60,000 to 180,000 miles per second. They possess much higher powers of penetration than α rays. Their velocities of ejection and consequently their penetrating powers vary within wide limits according to their origin, and they have been observed in air at considerable distances from their source, *e.g.*, 15 metres.

β rays are subdivided into "hard" β rays absorbed by 8 mm. of aluminium or 14 mm. of soft tissue, and "soft" β rays absorbed by 4 mm. of aluminium, or 7 mm. of soft tissue.

γ RAYS

γ rays represent 4.8 per cent. of the total energy of radium ; they are very penetrating rays, non-deviated by the magnetic field. They are never emitted alone by any radioactive substance, but always together with β rays. Unlike α and β rays which are material particles γ rays are high frequency vibrations. They travel at a rate of 186,000 miles per second, that is, the speed of light. Their power of penetration is greater than that of α and β rays, this property varies with the hardness, but for example the γ rays from radium C can penetrate 20 cm. of lead and still produce appreciable ionisation. One divides γ rays into "soft" and "hard". The soft γ rays are absorbed by 2 mm. of lead. When passing through the tissues of the body γ rays give rise to secondary β rays which possess a therapeutic value.

Radon or Emanation

The spontaneous emission of energy by radioactive substances is accompanied by a change in the substance giving off radiations. Radioactivity is an atomic property, independent of chemical combinations. The first product from disintegration of radium is radon or radium emanation.

The rate of destruction of radium is such that in 1700 years it loses 50 per cent. of its weight.

If radium is placed in a closed chamber it gives off radon gas at a definite rate. At the end of a month a maximum amount of radon has been given off and the radium salt and the radon are said to be in equilibrium. Equilibrium is attained when the amount of emanation destroyed in a unit of time is equal to the amount of emanation produced.

The quantity of emanation in equilibrium with 1 gm. of radium is the "Curie". When radon is separated from

the salt which gave rise to it it is spontaneously destroyed. Fifty per cent of the radioactivity disappears in 3.85 days. At the end of thirty days 99.55 per cent of the radon has disintegrated.

FILTRATION

The work of Dominici has made clear the advantage of filtering the rays used for therapeutic purposes. Various metal filters can be used. The object to be obtained is pure gamma-ray therapy, this necessitates the elimination of β rays and can be secured by enclosing the radium salt or radon employed in a sheath or tube of metal capable of absorbing the β rays. Table 1 shows the various metallic substances and their filtering powers.

Substance	Density	For Absorption of —	
		β Rays	99.9 β Rays
Aluminium	2.7	0.52 mm	5.2 mm
Brass	8.5	0.16	1.6 "
Copper	8.9	0.15	1.5 "
Silver	10.6	0.13	1.3 "
Lead	11.3	0.12	1.2 "
Gold	19.3	0.07 "	0.7 "
Platinum	21.5	0.06 "	0.6 "

Platinum represents the best filter, as 0.6 mm will absorb 99.9 per cent of β rays. The amount of γ rays which are filtered by various thicknesses of platinum is as follows —

0.3 mm of platinum screens 3.65 per cent of γ rays
 0.4 mm " " 4.84 " γ rays
 0.5 mm " " 6.01 " γ rays

The study of the action of radon has shown that β rays caused necrosis of the tissues in the vicinity of the focus of irradiation. The necrosis is in inverse proportion with the screenage. The poorer the screenage the greater the destruction. The field of tissue destroyed never extends beyond 8 mm² from the centre of irradiation. When

non-filtered radon is used, it becomes evident that the β rays are non-selective in their action and affect normal and malignant tissue in nearly equal degree, the result being radium necrosis, 0.5 mm. of platinum screens off β rays and the γ rays having a selective action on cancerous cells, necrosis is eliminated whilst destruction of malignant cells is still obtained. By increasing the thickness of platinum it is possible to utilise only γ rays of very short wave-length. The greater the quantity of radium employed in a given area of mass, the more necessary it becomes to provide adequate screenage.

RADIUM SALTS

The metallic radium isolated by Mme Curie is a white substance which cannot be conserved without alteration. For therapeutic purposes radium is used in the form of salts. Radium bromide, which is soluble, is used for the production of radon and radium sulphate for enclosure in containers. The strength of the radium salt is always expressed in terms of radium element. The radium element content of 1 mg of radium sulphate is 0.7; that of bromide (anhydrous) is 0.58. Or conversely 1 mg of radium element is contained in 1.4250 mg of radium sulphate and in 1.7072 mg of anhydrous radium bromide.

UNITS

The unit of radium is 1 gm of radium element. The therapeutic unit is 1 mg of radium element. The unit of radon is 1 curie, 1 curie is the quantity of emanation in equilibrium with 1 gm of radium.

The volume of 1 curie of radon at 0° C and at a pressure of 760 mm of mercury is 0.6 mm³. The practical unit is 1 millicurie. The unit of dose is either the milligram-hour or the millicurie. A milligram hour is the quantity of radiation given off by 1 mg of radium element in one hour.

1 millicurie destroyed = 132.38 mg. hours.

1 mg hour = 0.00755 millicurie.

A microcurie is $\frac{1}{1,000}$ of a millicurie.

1 gm of radium element in equilibrium produces per hour 755 millicuries of emanation and the same amount of emanation is destroyed in the same time

1 mg of radium element produces per hour 755 microcuries of emanation

0.6 mg of radium element gives an intensity of 5 microcuries per hour 1.33 mg of radium element give an intensity of 10 microcuries per hour

To convert milligramme hours into microcuries it is necessary to multiply the number of milligramme hours by 7.55 For instance —

5,000 mg hours = $5,000 \times 7.55 = 37,750$ microcuries =
37.75 millicuries destroyed

The Time Factor

The principle underlying modern radium therapy is that of prolonged irradiation with small doses. In calculating the dose in milligramme hours it is necessary to consider the time factor e.g. 100 mg applied for ten hours equals 1,000 mg hours

Fifty mg applied for twenty hours also equals 1,000 mg hours but the biological effect is different in the two cases. The biological effect varies also with the distance between the radium and the surface. To obtain a similar dose at a distance of 15 mm from the skin it is necessary to give the patient ten times the dose one would have given by interstitial irradiation. Hence, in calculating or noting the dosage in surface application it is necessary to give the following data —

- (1) Method of application
- (2) Amount of radium
- (3) Number of hours
- (4) Distance from the skin

It is useful to note the number of foci, e.g., total dose 8,000 mg hours (in twenty foci) in ten days at ten hours daily at a distance of 15 mm

To obtain the most effective irradiation it is necessary to prolong the time factor, this necessitates diminution

of strength of radium needles in interstitial methods or increase of distance between the area to be treated and the source of the gamma rays, in cases of surface application. Homogeneous irradiation is obtained by the use of numerous feeble foci. Regaud¹ obtained sterilisation of a ram's testis by prolonged irradiation with feeble doses of gamma rays, although he failed to do so by using three times the dose for a shorter period. From this experiment he concluded that the cells are more radio-resistant at certain stages of their life cycle than at others. The application of this observation to the treatment of cancer has given greatly improved results, and some forms of squamous celled carcinoma which were considered as radio-resistant have proved to be radio-sensitive with the improved method of prolonged irradiation.

REFERENCES

- 1 OWEN, E. A., and NAYLOR *Proc Phys Soc of London*, 1922
- 2 LACASSAGNE, A. "Recherche Experimentale sur l'action des rayonnements β et γ du radium agissant sur les tissus par radium puncture" *Journal de Rad et d'Electrolog* 1921, 5, p. 160
- 3 LABORDI, SIMONE "La Curietherapie des Cancers" Masson, 1925, p. 31
- 4 REGAUD, CL., LACASSAGNE, A., FERROLA, R. *Radiophysiology et Radiotherapy*, Vol. 1, fasc. 2, p. 179

CHAPTER II

METHODS OF IRRADIATION

THE object of radium treatment is to administer a lethal dose to each cell of the neoplasm. Cinti has shown very graphically in his film the effect of radium on sarcoma cells, mitosis stops and the cell disintegrates. In successful cases a lethal dose has been administered to all cells. A sublethal dose produces inhibition of growth for various periods of time in our experience even for so long a period as two and a half years. To obtain results clinically satisfactory it is necessary to give the whole neoplasm a homogeneous dose sufficient to produce the disintegration of the tumour with the least damage to the healthy surrounding tissues. It is evident that tumours of big volume situated deeply from the surface will present technical difficulties, although they may be of radiosensitive type. There are four methods of irradiation in use at present, of these the first three are in constant use at Westminster Hospital, the fourth is described, as it presents great possibilities for the future but up till now has been employed only at the Paris and Brussels Radium Institutes, and at the Memorial Hospital, New York.

(1) Cavity Method

This is applicable in certain cases of oral, rectal and vaginal cancer. The radium is introduced through the natural opening and maintained in position by means of holders which vary in construction according to the anatomical site. In the case of an epithelioma of the palate or cheek, *e.g.* a vulcanite apparatus similar to a denture is used carrying the requisite quantity of radium. This appliance is made individually for each patient (Figs 16 and 17). The application may be continuous or interrupted and is prolonged till the desired reaction is obtained.

In cases of vaginal or uterine cancer, a pessary or wax model is used (Fig. 40) This method is supplemented by radium puncture, but presents the advantage of simplicity and gives good palliative results

A rectal applicator of suitable size and made of rubber tubing offers a simple way of sterilisation as a preliminary to other methods of irradiation in selected cases of carcinoma of the rectum The cavitory method is of great simplicity, but its general use has been abandoned by most workers owing to the difficulty of distributing the irradiation equally throughout the lesion The palate and buccal aspect of the cheek are the only situations where this method is still used in preference to any other

(2) Interstitial Irradiation

This method consists in the introduction of radium salts or radon seeds suitably screened by platinum around and into the tumour. It is most suitable for those growths which are of small size and easily accessible to manipulation. The use of platinum needles of suitable length and strength and provided with trocar points and eyelets has become the method of choice in the treatment of lesions of the tongue, floor of the mouth and certain types of cancer of the breast, and secondary nodules after amputation of the breast. The needles are secured in position by means of sutures or ligatures, are retained for periods up to ten days or even more and are withdrawn at the end of the treatment by the thread attached to the eyelet In tumours of small volume it is sufficient to surround the lesion with needles ; in bigger ones it is useful to introduce the needles into the tumour as well The introduction of platinum screened radon seeds has extended the use of this method of interstitial irradiation to certain types of cancer of the œsophagus and stomach The advantages of this method in suitable cases are -

(1) The possibility of calculating the dose carefully and accurately

(2) Homogeneous irradiation.

(3) Prolongation of period of irradiation, since normal tissues are protected by the multiplicity of foci and maximum screenage

This method is not suitable for treatment of secondary lymphatic involvement and has been abandoned completely in the treatment of glandular cancer in the neck. In the treatment of cancer of the larynx it presents many advantages. In cases where the extent of the growth cannot be exactly appreciated clinically this method is not suitable

(3) Surface Application

By surface application is meant the application of radium at a short distance from the skin. The method of applying radium directly on the skin was discarded because the cutaneous reaction occurs before the optimum dose of irradiation to the underlying growth has been given. This method, as practised at Westminster Hospital, is based on the teaching and practice of Regaud. It differs from it chiefly in the distance at which the radium is placed. At Westminster Hospital 15 mm is the standard distance, in certain cases and for specific reasons a double distance is used, and occasionally 1 cm only. The standardisation of distance is useful if experience gained in a number of cases is to be employed for the calculation of dosage. The substance employed is that described by O Monod, A Esguerra and G Richard⁵. It is known as Columbia paste and has the following composition —

Beeswax, 100 gm
Paraffin (melting at 62° C) 100 gm
Fine white wood sawdust, 200 gm

Preparation of Columbia Paste

Beeswax and paraffin are melted together by gentle heat and well mixed. When thoroughly mixed it is allowed to cool slightly and the sawdust is added slowly, stirring continuously. This produces a spongy yellow mass which is allowed to cool till all the air bubbles disappear. When

the mixture is free from air bubbles it is heated again and vigorously stirred. It is then poured into clean flat glass dishes 15 mm high and allowed to cool. It is better to cool rapidly by immersing the dish in cold water. The plaque of Columbia paste presents one smooth pale yellow surface and one dark brown slightly granulated surface. Columbia paste has been adopted as a support for surface irradiation at the Radium Institute of Paris, after extensive trial of various compounds. It possesses the following properties —

- (1) It does not give rise to secondary radiations.
- (2) It gives a diffuse superficial distribution of the rays which is homogeneous
- (3) It is easily malleable at a temperature which is tolerated by the skin and is sufficiently hard at body temperature to keep its shape
- (4) It is easily kept clean and is fairly light in weight, even when applications of large size are necessary

Preparation of Apparatus

Heated to 48°C the paste becomes soft and malleable but not brittle, it can be handled with ease and suitable pieces cut out, these are accurately moulded over the part to be treated either directly or on a previously prepared plaster model. The sawdust surface is placed nearest to the skin. The model is then immersed in cold water and hardens rapidly. The next step is the disposition of the radium tubes or needles in the prepared Columbia paste apparatus. This can be done either by gently heating each tube or needle by passing it through a flame and applying it on to the external, yellow smooth surface of the apparatus, or by enclosing the needles between two layers of adhesive plaster and applying this to the paste.

Distribution of Needles on the Surface of the Wax Apparatus

To obtain a homogeneous irradiation it is advisable to use as many needles or tubes as will conveniently cover the surface to be treated. A large number of small needles

containing 0.6 mg., 1 mg., or 1.5 mg. of radium is preferable to a few tubes containing larger quantities. The needles are placed at a distance of 1 cm. or 0.5 cm. from each other. If the treatment is prolonged over two to four weeks it is advisable to redistribute the radium needles once a week, this helps to obtain homogeneous irradiation. Lead sheeting 1 mm. thick covered with a thin layer of rubber is incorporated in the apparatus or so applied to the surface of the plaque as to protect healthy tissue, especially the nose, the lobule of the ear, the orbit or the laryngeal cartilages. Additional safety may be secured by covering the external surface with a sheath of lead. The wax, radium and lead are strapped together by adhesive plaster so as to form one apparatus and guard against loss of needles. The apparatus must be maintained rigidly in position by means of bandages. The treatment may be continuous or intermittent, allowing a few hours' rest daily. It is, as a rule, tolerated by patients without undue discomfort for periods up to one month, the patients being encouraged to persevere with the treatment.

Types of Cases Suitable for Surface Application

This method is eminently suitable for the treatment of cervical secondary deposits, carcinoma of the breast, mediastinal or pulmonary new growth, brain tumours and intra abdominal neoplasms. It can be used in combination with the intersutural method of irradiation but should never be used simultaneously with it as otherwise secondary irradiation may lead to necrosis from an overdose.

Surface application has enormously extended the field of usefulness of radium therapy.

It is a wasteful form of applying radium as a great deal of irradiation is lost but it possesses many advantages. It requires no anæsthetic or operative procedure of any kind except in certain cases of pharyngeal growths and in cerebral cases. It can be prolonged for a sufficiently long period to give the biggest possible dose to tumours situated deep in the tissues or inside the abdomen or chest. The super

ficial reaction can be observed daily. Large areas can be irradiated at once. It is a more expensive method than needling, since it requires a larger quantity of radium.

(1) Distance Irradiation

This method in use in the Brussels ⁶ and Paris ⁷ Radium Institutes utilises large quantities of radium applied at distances of 10 cm. or more from the skin. It presents the same advantages as surface application, but much larger doses can be given without damaging the skin. The details of technique vary with the individual centres. It requires 4 or more gm. of radium and a special room for treatment. The radium is contained in a box suspended above the patient, the box is lined with lead and has a window to allow the rays to be directed on the patient. The apparatus weighs 150 lb., and by means of a system of pulleys or a trolley can be suspended at the desired angle and at the requisite distance from the patient. It has been used with good results in cases of cancer of the breast and uterus. The distance from the skin must be very carefully calculated. The patient receives two to three hours of irradiation daily for periods of two to three weeks. Multiple ports of entry are made use of so as to minimise the quantity of rays absorbed by any one area of skin. Distance irradiation presents the following advantages — ⁸

- (1) Greater penetration of the rays is obtained
- (2) Dosage can be increased very considerably without damage to normal tissues.
- (3) Treatment can be divided into daily sittings of short duration
- (4) The total treatment can be spread over longer periods of time

The disadvantages of the method are of economical order only, namely, initial expense for the acquisition of large quantities of radium and installation of a special treatment room.

The method has given results which outweigh all consideration of cost.

APPARATUS

Needles

The radium used at Westminster Hospital both for interstitial and surface therapy is distributed in needles and tubes

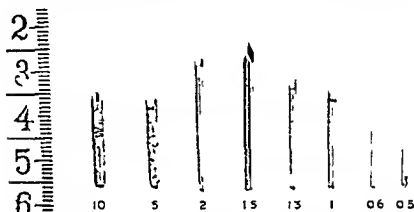


FIG 1 —PHOTOGRAPH OF NEEDLES IN USE AT WESTMINSTER HOSPITAL
The figures indicate the amount of radium in mgs contained in each needle

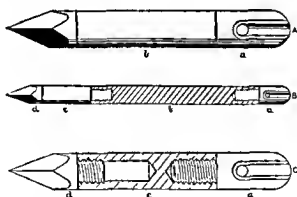


FIG 2 —DIAGRAM OF NEEDLES

A Needle composed of three sections —

a Eyelet—provided with groove for thread

b Body—radium carrying chamber

c Trocar point screwed on to body of needle

B and C Section of special needle devised by E Rock Carlin, F.R.C.S. Portion b is made of celluloid and is interposed between a and c. It is made in various lengths. The needle is extremely useful in cases where normal tissue has to be traversed before reaching the neoplasm. The eyelet a can be screwed on directly to c and the needle used in the same way as needle A.

The needles are made of platinum of various thicknesses according to the quantity of radium per needle. All needles have eyelets and trocar points.

ficial reaction can be observed daily. Large areas can be irradiated at once. It is a more expensive method than needling, since it requires a larger quantity of radium.

(4) Distance Irradiation

This method in use in the Brussels ⁶ and Paris ⁷ Radium Institutes utilises large quantities of radium applied at distances of 10 cm or more from the skin. It presents the same advantages as surface application, but much larger doses can be given without damaging the skin. The details of technique vary with the individual centres. It requires 4 or more gm of radium and a special room for treatment. The radium is contained in a box suspended above the patient, the box is lined with lead and has a window to allow the rays to be directed on the patient. The apparatus weighs 150 lb, and by means of a system of pulleys or a trolley can be suspended at the desired angle and at the requisite distance from the patient. It has been used with good results in cases of cancer of the breast and uterus. The distance from the skin must be very carefully calculated. The patient receives two to three hours of irradiation daily for periods of two to three weeks. Multiple ports of entry are made use of so as to minimise the quantity of rays absorbed by any one area of skin. Distance irradiation presents the following advantages — ⁸

(1) Greater penetration of the rays is obtained.

(2) Dosage can be increased very considerably without damage to normal tissues.

(3) Treatment can be divided into daily sittings of short duration.

(4) The total treatment can be spread over longer periods of time.

The disadvantages of the method are of economical order only, namely, initial expense for the acquisition of large quantities of radium and installation of a special treatment room.

The method has given results which outweigh all consideration of cost.

APPARATUS

Needles

The radium used at Westminster Hospital both for interstitial and surface therapy is distributed in needles and tubes

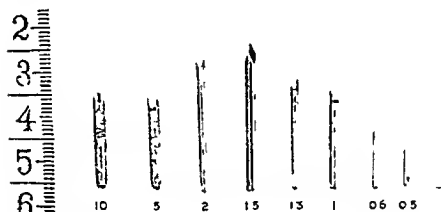


FIG 1—PHOTOGRAPH OF NEEDLES IN USE AT WESTMINSTER HOSPITAL
The figures indicate the amount of radium in mgs contained in each needle

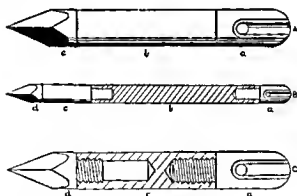


FIG 2—DIAGRAM OF NEEDLES

A Needle composed of three sections —

a Eyelet—provided with groove for thread

b Body—radium carrying chamber

c Trocar point screwed on to body of needle

B and C Section of special needle devised by E. Rock Carling, F.R.C.S. Portion b is made of celluloid and is interposed between a and c. It is made in various lengths. The needle is extremely useful in cases where normal tissue has to be traversed before reaching the neoplasm. The eyelet a can be screwed on directly to c and the needle used in the same way as needle A.

The needles are made of platinum of various thicknesses according to the quantity of radium per needle. All needles have eyelets and trocar points.

The following are details of specification of the needles (Figs. 1 and 2):—

Amount of Radium	Overall Length	Screenage— mg. of Platinum	Ext. Diameter
0.5 mg.	9 mm.	0.5	1.7 mm
0.6 "	16 "	0.5	1.6 "
1 "	24.5 "	0.8	2 "
1.33 "	27 "	0.6	1.8 "
1.5 "	33 "	1	2.6 "
2 "	33 "	0.65	1.9 "
5 "	22.5 "	1	2.65 "
10 "	21.1 "	1	2.8 "

Seeds

Seeds are capillary glass tubes filled with radon or emanation gas. The use of seeds has been advocated for several years in America, chiefly by Joseph Muir, but it is only for the past year or so that their use has become generalised in this country. The seeds used at Westminster Hospital are made by the Radium Institute, London.⁹ They are minute torpedo shaped platinum cases containing capillary glass tubes. Each seed is 6 mm. long, 1.4 mm. maximum thick and has a wall of 0.5 mm. of platinum. At one end of the seed is a fine thread. The dosage varies with the requirements of individual cases. Each seed, when implanted, contains 1.8 or 1.2 millicuries of radon. With 0.5 mm. of platinum screenage pure gamma irradiation is obtained. At the end of two weeks the seeds have no practical radioactive value. The seeds are introduced by means of a special trocar and canula (Fig. 3). They carry a thread which can be cut short before introduction of the seeds if their removal is not necessary.

The use of seeds presents the following advantages:—

- (1) Their introduction is more rapid and easier than that of needles.
- (2) They need not be sutured in place.
- (3) They can be used in situations where the insertion

of needles is impracticable, such as the pyriform fossa, stomach, œsophagus

(4) They can be left in permanently without loss of radium or damage to the patient

(5) Hospitalisation of patients is not necessary except when laparotomy or thoracotomy is performed

The action of seeds, however, is not identical with that of radium needles. The difference is one of intensity

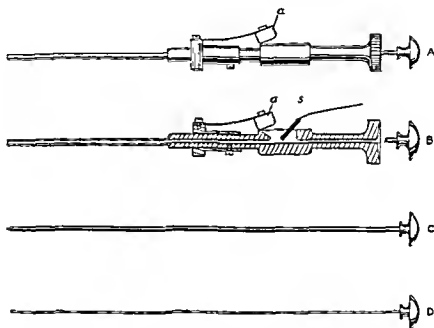


FIG 3—SEED INTRODUCER

A Canula shown in section in B. The trocar C is introduced into the canula. The clip *a* is movable. The seed *s* is placed into the slot and kept in position by clip *a*. When loaded the trocar and canula are introduced the desired depth. The trocar is removed and the stilette D pushes the seed along the canula into the tissues. The trocar is then withdrawn.

Whereas with needles irradiation of uniform intensity is obtained during the whole period of treatment, in the case of seeds a relatively large dose is given off during the first three days (50 per cent) the remainder being a progressively weaker dose.

In comparing the results obtained by the two methods in similar types of growth *e.g.* cancer of the floor of the mouth experience has shown that to obtain disappearance of similar lesions it is necessary to use very much bigger

initial doses of radon than of radium. To produce complete sterilisation of a growth the terminal period of treatment is as important if not more so than the initial period, and this is where the radon seeds differ from radium needles. The combined use of seeds and needles is sometimes of great practical utility. The disadvantages are overcome by careful dosage, adequate screenage and duplication of treatment.

REFERENCES

- 5 MONOD, O, ESGUERRA, A, and RICHARD, G "Generalités sur l'emploi des substances plastiques en Curiothérapie de surface" *Journal de Radiologie et d'Electrologie*, 1922, p 331
- 6 SLUYS and KESSLER, E "Gammatherapie" *Le Cancer* No 3, 1925, p 89 and No 4, p 150
- 7 BRUZAU, M, and FERROUX, R "Principes et dispositifs de la Curiothérapie à distance" *Le Cancer*, Special No, 1926, p 146
- 8 BRUZAU, M, and FERROUX, R "Arch de l'inst du Rad Fond Curie Radiophysiologie et Radiotherapy," 1928, Vol I, fasc 2, p 324
- 9 GOSSE, P, and CHESTER-WILLIAMS, F E "The screened Radon Seed in the Treatment of Malignant Disease" *The Lancet*, August 18th, 1928, p 323.

CHAPTER III

GENERAL PRINCIPLES OF RADIUM THERAPY

THE effect of irradiation on tissues is at present imperfectly understood. From histological studies of irradiated tissues it has been recognised from the earliest days of radium therapy that cells in mitosis are more sensitive to irradiation than cells at rest. Dominici¹⁰ showed as early as 1907 that cells are more sensitive to irradiation the more nearly they approach the embryonic state. Perthes¹¹ and Bohn¹² in independent experiments showed that the chromatine is the part of the cell most sensitive to irradiation.

These and other studies demonstrated that different cellular elements respond differently to the same dose of irradiation.

Bergonie and Tribondeau¹³ have formulated the law that the sensitivity of cells to irradiation is in direct proportion to the reproductive activity of the cells. The action of radium on cells or tissues may be summarised as follows:

(1) **Excitation of Activity** ^{14 15 16}—Numerous experiments by different workers during the past twenty years have given such contradictory results that it cannot at present be asserted or denied that radium even in very small doses produces an excitatory effect on tissue or stimulates growth.

(2) **Inhibition of Activity** ^{1 18 19 20 21}—This has been established quite definitely both by histological studies of irradiated tissues and by observations on tissue cultures *in vitro*. It finds also substantial proof in various clinical manifestations.

(3) **Destruction of Tissue**—This was the first known effect of radium on tissues. It has shown the possibilities of irradiation and has gradually led to modern radium therapy.

The destructive action of radium is subdivided by

Regaud ²² into two types, (1) Diffuse cytocaustic action ; (2) Selective cytolethal action.

The first is really a radium burn and is obtained by the action on the tissues of feebly penetrating rays acting for a sufficiently prolonged period of time. It is a lesion producing necrosis of all tissues affected without any selectivity.

The cytolethal action is obtained from an equal quantity of radium, provided that by means of suitable screenage rays of greater penetrating power alone are used. The screenage arrests β rays and the effect obtained by γ irradiation is essentially selective, it affects certain cells, whilst others appear to be immune to it ; it is not limited to the surface of the irradiated area, but extends deeply into the tissues.

EFFECT OF RADIUM ON THE SKIN

Erythema

When a sufficiently big dose of gamma rays has been administered to the skin a series of changes is observed. After three to four days the irradiated area becomes red and a sensation of heat and irritation is experienced ; this is known as the " erythema dose," and is used as a basis for dosage by many radiologists. In practice it is found that in the treatment of a malignant growth, by surface application, the erythema dose is not sufficient to produce the optimum results and a greater dose is compatible with safety. Erythema is generally followed by pigmentation and epilation.

Peeling Dose

If irradiation is prolonged beyond the stage of erythema the skin becomes darker, deep red or purple in colour ; on the tenth day blisters appear, and this is followed by peeling. About the fifteenth day the superficial layers of the skin have fallen off, leaving a moist, smooth, pinkish-grey surface in places covered with fibrin, but never oozing blood (Plates IX and XII)

This reaction has been called by Regaud "acute selective radio-dermatitis"²³ It is used as an index of dosage The skin heals rapidly (two to four weeks according to extent of peeling) by peripheral proliferation of epithelium which gradually covers the raw surface The skin when healed is pink, soft and healthy The whole process is painless To obtain this reaction with impunity it is essential to irradiate the tissues very slowly at a minimum distance of 15 mm from the skin and to screen the radium sufficiently to cut off all the β rays

Radium Burn

If a considerable dose of irradiation by means of insufficiently screened radium is administered rapidly an acute reaction results At the end of the third day the skin becomes red, œdematous and painful, blisters form rapidly, and when peeling follows the surface exposed is grey or green, œdema and pain increase and a slough forms which takes months to separate This is spoken of as radium necrosis, it is due to bad technique and should never occur The ulcer which follows the separation of the slough takes a very long time to heal

EFFECT OF IRRADIATION ON MALIGNANT CELLS

Malignant tumours are characterised by the rapid division of their constituent cells, which in certain characteristics resemble those of embryonic tissue They respond to irradiation more rapidly than normal tissues The higher the degree of differentiation of a cell the more sensitive it is to irradiation

Lacassagne and Monod²⁴ in Paris, and Canti and Donaldson²⁵ at St Bartholomew's Hospital and the Cambridge Research Hospital, have carried out histological investigations in cases of cancer of the cervix uteri treated by radium These investigations show that mitosis disappears immediately after irradiation, but reappears a few days later in abnormal forms The following abnormalities are

noted: Irregularity in the arrangement of chromosomes, disorganisation of the spindle, multipolar division. This abnormal activity ceases about the sixth day and is followed by disintegration of the cells. The effect of radium on mitosis and proliferation of cells was studied also by Champy ²⁶

Canti's cinema film shows better than any description the arrest of mitosis produced by radium in normal and malignant cells.

EFFECT OF IRRADIATION ON THE STROMA

Roussy has pointed out the importance of the condition of the connective tissue stroma on the effects of irradiation on tumours. The stroma plays an important part in the response of the tumour to irradiation. It has been shown both in histological study of irradiated malignant growths and in observation on tissue culture that the stroma has a restraining influence on the proliferation of cells. Roussy ²⁷ describes three types of reaction

(1) **Efficient Reaction.**—Characterised by the presence of normal blood vessels, the appearance of plasma cells and fibroblasts and the disappearance of small round cells. This terminates in fibrosis

(2) **Deficient Reaction.**—Characterised by œdema of the stroma, the presence of polynuclear neutrophil cells and abnormally thin-walled blood vessels.

(3) **Indifferent Reaction.**—Showing a mixed histological picture containing features of (1) and (2). From the microscopical examination of numerous sections made at frequent intervals during and after irradiation, Roussy draws the conclusion that the response of the tumour to irradiation depends not only on the effect on the cells, but equally on the effect on the stroma. A good result may be expected in those cases where disappearance of mitosis and cellular disintegration is unaccompanied by changes in the stroma. A bad result may be expected if the stroma is affected although the cells remain unchanged. It is possible to give an accurate prognosis in cases where

disappearance of cells is accompanied by marked changes in the stroma.

Personal observations^{8, 9} on biopsies in cases of lingual cancer fully support Roussy's observations, and prognosis is found to be bad in cases where the tissues are adenomatous.

MECHANISM OF THE ACTION OF RADIUM

The methods by which these changes are produced are at present not known. There is an obvious local effect of irradiation both on the cells and the sustaining tissue. This local action is seen clinically and microscopically. It is possible that this local action is a direct response of the cells to the gamma rays. Regaud¹⁰ presumes that the rays act indirectly on the cells by the production in the plasma of toxic substances which are responsible for the changes observed. It is true that the effects of irradiation on the tissues are partly dependent on the blood and lymph supply of the tissues and that this influences materially the results obtained from gamma ray therapy. Regaud's theory finds support in the work of Dustin¹¹ who describes the similarity of the effects of radiations and that of certain toxic substances named by him "erythroclastic poisons" on the sensitive chromatin of the cells at certain stages of activity. Experimental evidence as to direct or indirect action is at present not conclusive. Between the time of irradiation and the appearance of the changes a period elapses which varies with several factors. Thus "latent period" is of clinical importance as both malignant cells and normal tissue, although apparently not affected at the end of treatment, have been profoundly and permanently affected, the outward change not becoming apparent for a considerable time. The importance of the latent period is seen clinically in cases where skin previously irradiated may from small trauma, such as heat, cold or injury, break down and ulcerate rapidly even years after irradiation. Experimentally it has been shown by Bohm,¹² who irradiates frog's eyes and observed no changes till the stage of "blastula" is reached, when the whole structure degenerates.

noted: Irregularity in the arrangement of chromosomes, disorganisation of the spindle, multipolar division. This abnormal activity ceases about the sixth day and is followed by disintegration of the cells. The effect of radium on mitosis and proliferation of cells was studied also by Champy.²⁶

Canti's cinema film shows better than any description the arrest of mitosis produced by radium in normal and malignant cells.

EFFECT OF IRRADIATION ON THE STROMA

Roussy has pointed out the importance of the condition of the connective tissue stroma on the effects of irradiation on tumours. The stroma plays an important part in the response of the tumour to irradiation. It has been shown both in histological study of irradiated malignant growths and in observation on tissue culture that the stroma has a restraining influence on the proliferation of cells. Roussy²⁷ describes three types of reaction.

(1) **Efficient Reaction.** Characterised by the presence of normal blood vessels, the appearance of plasma cells and fibroblasts and the disappearance of small round cells. This terminates in fibrosis.

(2) **Deficient Reaction.** Characterised by oedema of the stroma, the presence of polynuclear neutrophil cells and abnormally thin-walled blood vessels.

(3) **Indifferent Reaction.** Showing a mixed histological picture containing features of (1) and (2). From the microscopical examination of numerous sections made at frequent intervals during and after irradiation, Roussy draws the conclusion that the response of the tumour to irradiation depends not only on the effect on the cells, but equally on the effect on the stroma. A good result may be expected in those cases where disappearance of mitosis and cellular disintegration is unaccompanied by changes in the stroma. A bad result may be expected if the stroma is affected although the cells remain unchanged. It is not possible to give an accurate prognosis in cases where the

Although at present we rely entirely on the local effect of radium, it is possible that in the future radium therapy may offer either alone or in combination with activating agents a form of serum therapy.

GENERAL EFFECTS ON PATIENTS OBSERVED DURING IRRADIATION BY γ RAYS

No disturbances comparable to those observed during treatment with intensive X-rays are observed. In cases of carcinoma of the mouth, where the dose of radium is small, no somatic changes due to the radium application are observed. In cases of surface application over wide areas, *e.g.*, breast, neck, abdomen, the following changes are noticed —

(1) A diminution in the total quantity of urine passed is noticed during the first three to four days of treatment, after that in those patients in whom a beneficial effect of the irradiation is observed clinically there is a definite polyuria.

(2) There is a rise in the pulse and respiration rates after the first twenty-four hours of treatment persisting for a week or more.

(3) Anorexia, general depression and slight malaise are observed in the majority of cases.

(4) No marked changes in the blood are elicited.

(5) In a few cases where the mass of growth acted upon by radium is of considerable size or in cases where numerous radon seeds are introduced into the œsophagus or intraperitoneally, marked toxic reactions characterised by a fall of blood pressure, vomiting, subnormal temperature and collapse are sometimes observed. These phenomena are allied to a form of protein shock produced by endogenous intoxication from the cellular elements of the irradiated tumour. This view finds support in the work of Loeper and Tonnet³⁹ who found a rapid increase of globulin, lipoids and glucose in the blood in cases of disappearance of tumours after irradiation. Clinically these manifestations comparable to anaphylaxis are found when a large

dose of radium is administered rapidly as in the use of radon seeds, where half the dosage is obtained in the first three days. The phenomena are less frequent and less pronounced if the treatment is prolonged over a long period, *e g*, two to three weeks. It is therefore an advantage to substitute surface irradiation for interstitial irradiation or to combine the two so as to minimise the latter when large masses of malignant growth are to be destroyed.

REFERENCES

- 10 DOMINICI, H "Modifications histologiques déterminées par le rayonnement du radium" IX^e Congrès de Med de Paris *Arch d'Elect Med* 1907, 15, p 835
- 11 PERTHES, G "Versuche über den einfluss der Rontgenstrahlen und Radiumstrahlen auf die Zellteilung" *Dent Med Woch*, 1904, pp 632-668
- 12 BOHN, G "Influence du radium sur les animaux en voie de croissance" *C R Acad des Sciences*, 1903, 136, p 1012
- 13 BERGONIÉ, J, and TRIBONDEAU, L "Premières expériences sur le rat blanc" *C R Soc de Biol*, Vol LVII, pp 400, 592, 595 (1904)
- 14 MALDINEY and THOUVENAIN "De l'influence des rayons X sur la germination" *C R Acad des Sciences*, 126, p 548, 1898
- 15 LAZARUS-BARLOW, W S, and BONNEY, V "The influence of radio-activity on the Division of Animal Cells" *Arch Middl Hospital*, 1909, 15, p 147
- 16 PRICE-JONES, C, and MOTTRAM J C "A Contribution to the Study of in-vitro Plasma Cultures of Mouse Carcinoma and Rat Sarcoma" *Arch Middl Hospital*, 1914, 33, p 21
- 17 REGAUD, CL, and LACASSAGNE, A "Action des radiations sur l'ovaire" *Arch de l'inst du Rad Radiophysologie et Radiotherapy*, fas 1, Vol I, pp 43-50
- 18 CANTI, R G Cinema Film
- 19 CANTI, R G, and DONALDSON, M "The Effect of Radium on Mitosis in vitro" *Proc Royal Soc B*, Vol C, 1926
- 20 CANTI, R G "The Effect of Irradiation on Tissues" *St Bart's Hosp Report*, 1927, pp 57-72
- 21 FINZI, N S "Treatment by Gamma Rays of Radium" *St Bart's Hosp Report*, 1927, p 74
- 22 REGAUD, CL, and LACASSAGNE, A *Radiophysologie et Radiotherapy*, Vol I, fas 1, p 3
- 23 REGAUD CL, and LACASSAGNE, A *Ibid*, p 17
- 24 LACASSAGNE, A, and MONOD, O "Les caryocinèses atypiques provoquées dans les cellules cancéreuses par les rayons X et γ et leur rôle dans la répression des tumeurs malignes irradiées" *Arch fr de path*, 1922 (Doin), fas 1
- 25 DONALDSON, M "The Radium Treatment of Carcinoma of the Cervix since 1921" *St Bart's Hosp Report*, 1927, p 104
- 26 CHAMPY, CH "Culture des tissus et tumeurs" *Bull Assoc Française pour l'Et du Cancer*, Paris, 1921

- 27 ROUSSY G De l'action des radiations dans le traitement des
Cancers *Le Cancer* 1926 Special No p 110
- 28 LAANS A and CADE S Cancer of the Tongue Preliminary
Report on Radium Treatment *British Journal of Surgery* Vol XX,
No 57 1927
- 29 CADE STANFORD Clinical Report on Cases of Carcinoma treated
by Radium *Annual Report British Empire Cancer Campaign*
1927-28 p 60
- 30 REGAUD CL Sur la radio immunisation des tissus cancéreux et
sur le mécanisme de l'action des rayons du radium sur les cellules
et les tissus vivants en général *Bull Acad Med* 1924 91
p 604
- 31 DUSTIN A P Etude comparative entre l'action des radiations et
l'action des poisons carvoclasiques *Le Cancer* Special No 1926
p 117
- 32 BOHN G Influence des rayons du radium sur œufs vierges et
secondee et sur les premiers stades du développement *C R Acad
des Sciences* 1903 136 p 1085
- 33 GUILLEMINOT H Action du radium sur la graine et le développe-
ment des plantes *Arch Flect Med* 1907 14 p 592
- 34 REGAUD CL et DURREUIL G Perturbations dans le dévelop des
œufs secondee par des spermatozoïdes röntgenises chez le lapin
C R Soc de Biol 1908 p 1014
- 35 LITTLE C C and BAGG H J The Occurrence of Two Heritable
Types of Abnormality among the Descendants of X rayed Mice
The Amer Journal of Rontg and Rad Therapy 1923 10 p 975
- 36 MURPHY J B Congres du Cancer Strasburg July 1923 *Comp
Rendus* p 74
- 37 SLOSSE and RLDING Etude des alterations humorales dans le
Cancer et le precancer *Le Cancer* 1925 No 4, p 442
- 38 WATERMAN N La cytolise des cellules cancéreuses et sa regula-
tion reticulo endotheliale *Le Cancer* 1927 No 3 p 381
- 39 LOEPER M and TONNET J Sur quelques variations chimiques
du sang apr s radiotherapie des tumeurs *Assoc fr p l etude du
cancer* 1923 No 2

CHAPTER IV

CANCER OF THE BUCCAL CAVITY

TONGUE AND FLOOR OF THE MOUTH

IN considering the relative values of surgery and radium therapy in the treatment of cancer of the oral cavity and tongue, one is faced with a problem of particular difficulty. Although it is comparatively easy, by means of radium, to obtain the disappearance of the primary growth in the mouth, the treatment of the cervical glands presents difficulties which can be overcome up till the present day only by a combination of surgery and radium therapy.

The purely surgical treatment of the primary lesion in the mouth is associated with a percentage of fatal results increasing in direct ratio with the extent of the growth. It is followed by a grave mutilation of the patient and finally, owing to the appearance of metastasis in a vast proportion of cases, and to local recurrence, the percentage of cures is small and the prognosis grave. To-day, surgical treatment stands where Butlin left it some thirty years ago. Further experience has led to the adoption of diathermy, as advocated first by Nagelschmidt, instead of the knife. This method was developed by Douglas Harmer,⁴⁰ and it extended the field of active treatment to a group of cases considered up till then as inoperable, and holds a definite and very useful place in the treatment of oral cancer. The application of radium treatment to neoplasms of the mouth produced only poor results at first, and it was only after the original, ingenious and persistent efforts of Quick⁴¹ in America and Regaud⁴² in France, that the possibilities of this method were made known.

The superiority of radium treatment is such that, as far as the primary growth is concerned, it is the only method which combines both safety in the actual performance



PLATE I

Epithelioma of Tongue

- A Before treatment
- B Five weeks after treatment
- C Four months after treatment

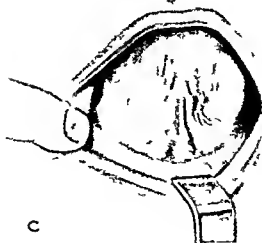
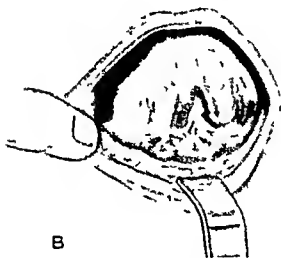
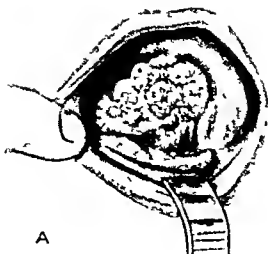
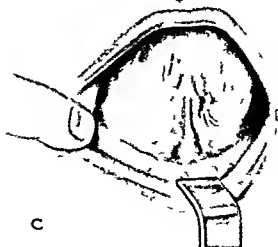
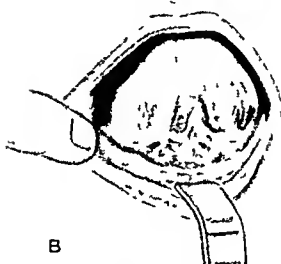
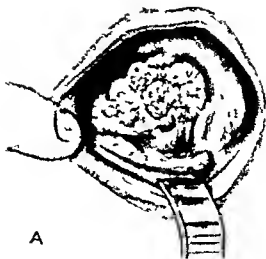


PLATE I

Epithelioma of Tongue

- A Before treatment
- B Five weeks after treatment
- C Four months after treatment



with the best results to be obtained, and this without mutilation

Surgical treatment in the hands of conscientious and skilled surgeons has given results so indifferent that those obtained by radium appear brilliant

In operable cases the immediate results are so good that, given the correct technique, this newer and more humane method of treatment ought gradually to supersede the older methods. As regards final cures, periods of eight years have now been passed. At Westminster Hospital patients treated as long as four and a half years ago are alive and well, so that it can be confidently expected that ultimate results will be as gratifying as the immediate alleviation offered to the patient.

Radium treatment does not always result in complete disappearance of the growth. In my experience a second treatment is possible and sometimes gives excellent results. Harmer advocates excision of the scarred tissue by diathermy. If treatment by radium has failed it in no way makes the case inoperable, on the contrary it often happens that an inoperable growth becomes operable.

PATHOLOGICAL CONSIDERATIONS

As the treatment of oral neoplasms by means of radium depends, at least partly, on the selective action of the gamma rays upon the newly developed cells it is important to give a brief outline of the pathological varieties which are submitted to these irradiations. The common type of malignant growth in the mouth is the squamous-celled carcinoma. Starting on the surface the epithelial cells grow downwards into adjoining tissues in columns of newly formed cells separated by a varied amount of fibrous tissue. The various stages of chronic superficial glossitis, so aptly called precancerous influence both the development of the neoplasms and the effects of treatment. The success of radium treatment depends upon the condition of the tissues bearing the neoplasm. Old-standing glossitis or syphilitic changes predispose to fibrosis and lead to changes

in the blood vessels and lymphatics of the tongue. As the best results are obtained in those cases where the blood supply is the richest and the lymphatic drainage freest, the condition of the stroma of the new growth is of the utmost practical importance. The presence of œdema is of the gravest import and the prognosis is frankly bad in those cases where the œdema is considerable. Clinically four types of neoplasm are recognised: the papillary, the nodular, the ulcerous and the fissured. The degree of malignancy of these groups when considered from the surgical point of view is in the order mentioned. From the point of view of radium therapy the prognosis is in the reversed order and the papillary type which is the most malignant responds most rapidly to irradiation. The more rapidly the tumour grows the more sensitive are the individual cells of the neoplasm to the effect of gamma rays. Clinically, it is found that the caryokinetic index of de Nabias is of less importance than the condition of the stroma.

ANATOMICAL CONSIDERATIONS

The anatomical situation of the primary growth affects the results obtained. The most favourable situation is the anterior part of the tongue or the lateral margin, the least favourable is the floor of the mouth. The posterior part of the tongue presents difficulties in approach, and so the extent of the lesion is easily underestimated. It also adds to the difficulty of the technique, but this is gradually being overcome by the use of special introducers and better illumination. The main reason why cancer of the posterior part of the tongue presents such difficulties is because the growths are nearly always advanced.

Growths of the inferior aspect of the tongue and floor of the mouth extend early beyond the intrinsic muscles of the tongue into the submaxillary and submental areas; they involve the alveolar margins and later on bone. This renders treatment difficult and necrosis is apt to occur. Early lesions in the floor of the mouth give good results.

The prognosis in radium treatment of cancer of the tongue depends upon three distinct factors (1) The anatomical situation and extent of the growth (2) The macroscopical variety of the tumour (3) The condition of the stroma and absence of œdema. The remainder of the oral cavity presents less difficulties. The palate, uvula, pillars of the fauces and buccal mucosa, when the seat of squamous-celled carcinoma, respond to radium treatment. The growths in these situations can nearly always be improved and sometimes disappear entirely. In the former case diathermy will often complete the cure.

LYMPHATIC DRAINAGE AND GLANDULAR INVOLVEMENT

The early involvement of the lymphatic glands and the difficulties presented by the treatment of the neck overshadow in importance all other considerations in dealing with the new growths of the oral cavity. It is the lymphatic invasion here, as in other situations, that is likely to defeat the efforts both of surgery and radium therapy.

The lymphatics of the tongue extend from the base of the skull to the clavicle, and form two longitudinal chains along the course of the main vessels of the neck and a semicircular chain comprising the submaxillary, submental and suprahyoid glands. The early involvement of the glands from carcinoma of the tongue and palate contrasts very unfavourably with the slower involvement of the glands in certain neoplasms of the lip and cheek.

The possibility of a bilateral invasion of the glands in a strictly unilateral growth is explained on anatomical grounds, and the bilateral infection in cases of neoplasms of the palate and frenum of the tongue is universally recognised. These factors must be taken into consideration when planning the treatment of a given case.

The suitability of a case for radium treatment and the choice of the technique to be adopted depends upon two principal factors (1) The degree of extension of the lesion (2) The anatomical position of the lesion. The question of glandular involvement does not *per se* materially alter

the treatment of the primary growth, although it profoundly affects the prognosis and demands a more careful consideration of dosage. Even with obvious glandular infection the primary growth can be made to disappear, and the question of the treatment of the lymphatic area presents a separate problem.

TREATMENT

The treatment of oral cancer is twofold: (1) Radium therapy of the primary growth, this should always be the first step; if it fails, surgery may still be resorted to. (2) The treatment of the lymphatic area. It has been stated repeatedly that it is advisable to treat the neck first, and it was argued in favour of this method of procedure that the radium applied to the primary lesion in the mouth had an activating effect upon the cells in the cervical lymphatics. This was based on the clinical observation that during the treatment of the tongue or palate by radium the cervical glands increased in size. The observation is probably correct, but its significance has been wrongly interpreted. The increase in size cannot be ascribed to the activating effect of radium upon distant neoplasm cells. Both clinically and from the observation of Cantl it is seen that the effect of radium upon neoplastic cells is inhibitory. The increase in size of the cervical lymphatics occurs only in cases where pre-existing oral sepsis has not been eradicated and is inflammatory in nature. It can, and ought, to be avoided by an adequate oral toilet and the sacrifice of all teeth even when apparently healthy. It is the custom at Westminster Hospital to treat the primary lesion first, allowing a period of three weeks between the treatment of the primary growth and the treatment of the cervical area. The reasons for treating this lymphatic area clinically gives satisfactory results on the basis of preserving the best to the area treated. It is hampered by the presence of blood vessels.

11

12

13

14

15

16

17

18

19

PLATE II

- A Epithelioma of Tongue Ulcerative type before treatment
B Twenty-one days after treatment.

PLATE II



A



B

tion on the neck. This step, therefore, should be left till the primary growth has been successfully dealt with. The only case in which the lymphatic area should be dealt with first is a lesion of the pyriform fossa.

Mode of Disappearance of the Growth

The tumour becomes softer and the surface of the growth and adjoining tissues takes on a whitish appearance as if it had been painted with pure carbolic acid (Plate I, *b*), the white layer is a deposit of fibrin, and is an indication that an optimum dose of radium has been given. The growth becomes flattened, the induration diminishes, and epithelialisation takes place from the periphery. With correct technique the amount of residual fibrosis is very small, and in successful cases it is difficult within three months of the cessation of treatment to find the site of the original growth.

Primary-Lesion Technique

The method employed in the treatment of the primary lesion in the mouth is based on the principle of prolonged irradiation with small quantities of well-screened radium. The older methods which aimed at rapid sterilisation of the growth by large quantities of insufficiently screened radium presented two disadvantages. The short period of treatment necessitated larger doses of radium and less protection, which resulted not infrequently in radium necrosis both of the soft parts and of the bones. The second disadvantage was that during the brief period of irradiation the cells not undergoing mitosis escaped the lethal dose and after a time became active again. The scars resulting from rapid irradiation are considerable. Before introducing radium it is essential to carry out a scrupulous toilet of the mouth. All carious teeth are extracted, tartar is scraped, gold bridges and metal fillings are removed so as to avoid secondary radiations which may lead to necrosis. Infection of the mouth is dealt with and

frequent mouth washes employed till the gums are healed. The introduction of radium needles can be carried out under regional anaesthesia if the patient is temperamentally suitable for it. For lesions on the postero-dorsal aspect of the tongue, intratracheal anaesthesia through a nasal catheter is preferable. The tongue is dried and examined by inspection and palpation, so that both the extent and the volume of the growth are ascertained. Needles are intro-

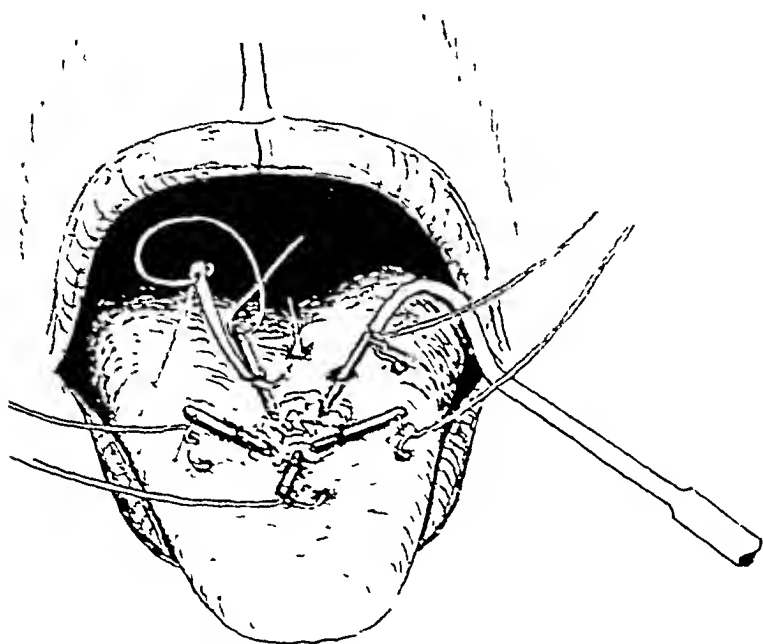


FIG. 4.—METHOD OF INTRODUCTION OF RADIUM NEEDLES

The linen thread is passed through the eyelet of the radium needle and tied. One end is passed through healthy tissue by means of an ordinary needle and tied. The needles are shown half introduced into the tongue but should be entirely buried.

duced around the growth into healthy tissue at a minimum distance of 1 cm. from each other (Fig. 4). The needles must be completely buried in the substance of the tongue, the linen thread only protruding at the surface, as otherwise small areas of superficial necrosis will occur around the protruding eye of the needle, although this part does not contain radium (Fig. 5). The thread is passed through the substance of the tongue, tied at one end and cut short. The long ends are collected into a rubber tube and attached

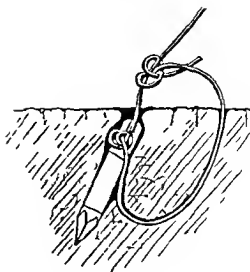


FIG 5

The radium needle is completely buried in healthy tissue around the neoplasm the thread protruding at the surface

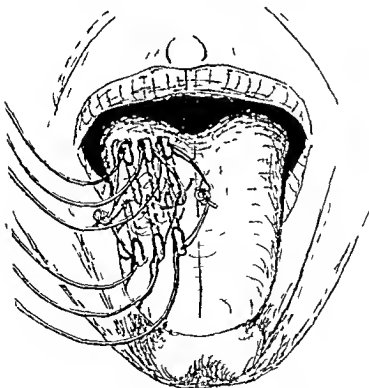


FIG 6 —ALTERNATIVE METHOD OF INTRODUCTION OF RADIUM NEEDLES

The needles are shown half introduced they should be entirely buried. They are not sutured to the tongue but attached to each other in couples. One end of the thread is left long.

to the skin of the cheek by means of strapping. An alternative method applicable to certain types of lesion and which obviates the necessity of suturing the needle into the tongue, is that described by Douglas Harmer.¹³ Longer needles are employed, "they are inserted into the growth itself and into normal tissue around it. In some cases more than one layer of needles is necessary. To keep them in position they are inserted in pairs, one needle being pushed from before backwards and the other from the reverse



FIG 7—Sialogram of T₁ REMOVABLE PLATINUM SEEDS IN TONGUE AND FLOOR OF MOUTH

direction (Fig 6). The linen threads which are attached to them are then tied together. With this method it rarely happens that a needle slips out of place." When dealing with a neoplasm situated far back on the postero-dorsal aspect of the tongue, the introduction of needles may present serious technical difficulties. In this position platinum radon seeds as made at the Radium Institute, London, are of great advantage (Fig 7). There are many technical advantages in favour of the use of seeds, most of which have been reviewed in Chapter II. It may be useful

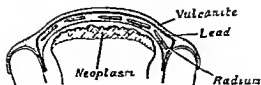


FIG 8—METHOD OF SURFACE IRRADIATION OF TONGUE

A vulcanite plate is applied on the alveolar margin; the plate carries a box containing radium and covered with 1 mm of lead so as to protect the alveolar border and the palate; the box covers the anterior portion and lateral margins of the tongue and extends backwards beyond the growth.

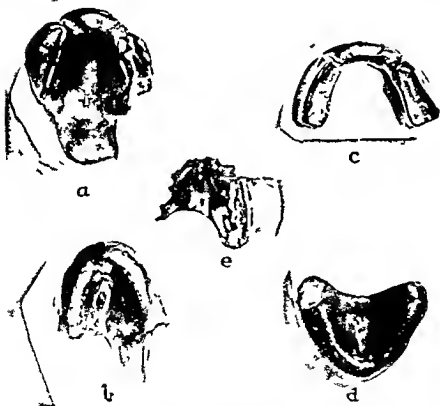


FIG 9—PLATES MADE FROM STENT OR SHELLAC LINED WITH 1 MM OF LEAD

a and b For protection of hard palate with extension backward to cover the lesion and keep needles in position.

c Plate for protection of alveolar margin of lower jaw during treatment of tongue.

d Plate for protection of palate and alveolar margin of upper jaw during treatment of tongue.

e Plate carrying small box lined with lead on inner side filled with Columbia paste and containing radium for treatment of epithelioma of cheek.

to recapitulate them here for cancer of the oral cavity, seeds are suitable because of the ease of their introduction and the fact that they need not be sutured in. They can be placed and kept in position in situations inaccessible to needles. In cases where an anæsthetic is undesirable seeds are to be preferred, as the time of introduction is shorter than that for needles. But from the point of view of uniform irradiation needles are superior, the dosage and especially the terminal irradiation are more under control. With adequate protection with platinum, seeds may be used in the oral cavity without lead protection of the bony arches, as the amount of irradiation emitted diminishes rapidly in the first forty-eight hours. In cases where most of the tongue is involved by the disease and the introduction of needles is difficult, surface application by means of an intrabuccal apparatus is an alternative although less efficient method of applying radium (Fig 8). The protection of the rest of the mouth, especially the palate and the upper and lower alveoli, is obtained by means of a dental apparatus made of vulcanite or stent and containing 1 mm of lead. The apparatus is made for each individual case, and the extent of the lead protection can be modified so as to leave a greater or lesser area of mucosa exposed to the rays (Fig 9).

Dosage

Needles containing 0.6 mg and 1.33 mg are used. Their number varies with the extent of the growth, with a minimum space of 1 cm between adjacent needles eight to ten needles are required to surround the neoplasm. The needles are left in position seven to eight days; very occasionally nine days are required to obtain the necessary reaction. The total dose varies from 800 to 1,600 mg hours. In a few cases as much as 2,600 mg. hours is necessary. If radon seeds are employed eight to ten seeds of 1.8 M.C. initial strength are left in position for ten days.

Causes of Failure in Treatment of the Primary Growth.—An analysis of the cases where the primary growth

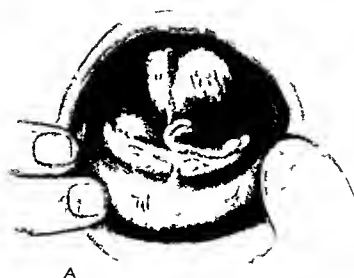
PLATE III

Epithelioma of Floor of Mouth and Tongue Ulcerative type

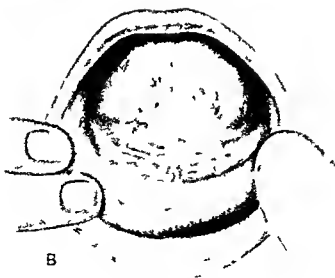
A Before treatment

B Two months after treatment

II VTF III



A



B

failed to respond to treatment shows that the cause of failure can be classified under four headings —

(1) Underestimation of the extent of the growth—this occurs chiefly in the postero-lateral group of lingual cancers, the extent of the disease is not sufficiently appreciated and the tonsillar portions of the growth are not subjected to irradiation

(2) Insufficient dosage Especially in situations pre-



FIG 10—BIOPSY OF CARCINOMA OF TONGUE ILLUSTRATED IN
PLATE —

Photo micrograph of squamous celled carcinoma Magnification
80 diameters

senting difficulties in access, the distribution of the needles is not sufficiently accurate, and the actual dose given is sublethal

(3) Radio-necrosis due to insufficient protection or to too large dosage in each needle

(4) Presence of oedema

Except for the last cause, where the reaction between tissues and radium is inadequate the causes of failures are avoidable by improvement of technique

Besides these causes of failure, a small number of cases appear to respond very inadequately to irradiation. Harner believes it to be due to a general constitutional factor, and he has noticed that in patients who have been alcoholics or have lived in hot climates, the results are not satisfactory.

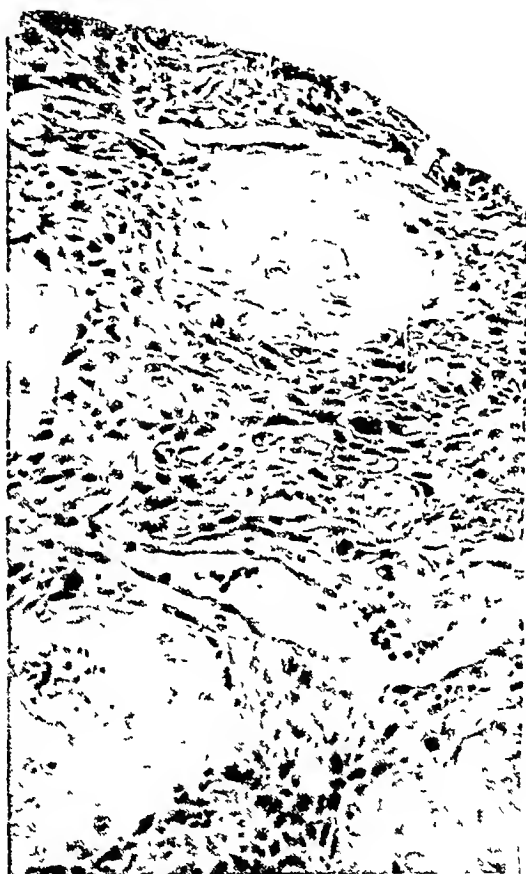


FIG 11

The same as Fig 10, magnified 300 diameters

The treatment of the cervical lymphatic areas is considered in Chapter V.

ILLUSTRATIVE CASES

Mr. F. A. V., age thirty-nine years Six months' history Epithelioma of the papilliferous type on the right border and on the under surface of the tongue, involving slightly floor of the mouth

Biopsy.—Squamous-celled carcinoma

Treatment—Twelve needles at 0.5 mg of radium element each and three needles at 1 mg each, inserted for seven days

Total Dose — 1 512 mg hours

(See Plate I)

- (a) Condition before treatment
- (b) Condition five weeks after treatment
- (c) Condition four months after treatment

There was a mass of glands on the right side of the neck A



FIG 12

The same as Figs 10 and 11 magnified 1 000 diameters

Cribe's dissection was performed three weeks after irradiation of the primary lesion and this was followed by a radium collar two months after operation

Total Dose to Neck — 12 000 mg hours No recurrence up till the present (ten months)

Mr M Ch age fifty nine years Epithelioma of floor of mouth and left lateral aspect of tongue and frenum Ulcerative type

Three months' duration Ten radon seeds introduced Total dose 18 M C D.

Palpable glands on the right side of the neck Crile's dissection performed No evidence of malignancy in glands on histological examination Complete recovery Well one year (Fig 7)

Mr H H , age forty-six years (Plate II) Extensive epitheliomatous ulcer on left side of tongue from tip to pillar of fauces, in-



FIG 13

Case under the care of Mr Rock Carling Epithelioma of the tongue
Condition before treatment

involving half the tongue Wassermann reaction positive No enlarged cervical glands

Biopsy —Squamous-celled carcinoma (Figs 10, 11, 12)

Treatment —Eleven needles at 0.6 mg of radium element each inserted around the growth for seven days Total dose, 1,108 mg hours The growth had entirely disappeared Well two years

Mr E F , age fifty-one Extensive epithelioma of the floor of mouth and right postero-lateral aspect of the tongue, tongue fixed, salivation very marked, pain in the ear, mass of glands in the right submaxillary and carotid areas

Nine needles at 0.6 mg of radium element and three needles at 1.3 mg of radium element introduced. Duration of treatment nine days. Total dose, 2,600 mg hours. Rapid retrogression of the disease. One month after radium treatment Crile's dissection performed. On leaving hospital slight induration on the lateral border of the tongue. No ulceration. no pain (recent case) (Fig 13)

Mr Wm C age forty nine years (Plate III). Seven months history of ulceration of floor of mouth. Epithelioma of left antero-

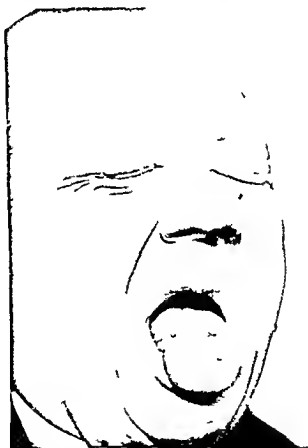


FIG 14

Same as Fig 13 Twelve months after treatment

lateral part of the tongue and floor of mouth. Mass of glands in submental and submaxillary regions.

Biopsy—Squamous celled carcinoma

Treatment—Eight needles at 0.6 mg of radium element each introduced for seven days. Total dose 806 mg hours. Lesion healed entirely within fourteen days. Crile's dissection on left side of neck. Recurrence of glands on right side of neck. Removal of glands (not a Crile's dissection). Recurrence of cervical deposits on right side. Death.

Mr C G II, age fifty-nine years (Plate IV) Epithelioma of dorsum of tongue, centrally situated extending down to but not involving floor of mouth No palpable glands.

Biopsy—Squamous-celled carcinoma

Treatment—Four needles at 1.3 mg of radium element each and six needles at 0.6 mg of radium element each, introduced for seven days Total dose, 1,478 mg hours Scar excised by diathermy three months after irradiation

Histology—Fibrous tissue only

Eight months later enlargement of cervical glands on the right side Crile's dissection performed Glands contained secondary



FIG 15—SKIAGRAM OF TWELVE RADIUM NEEDLES IN TONGUE AND FLOOR OF MOUTH

deposits Post-operative irradiation 10,000 mg hours Well twelve months

Mr A D, age seventy-three years (Fig 13) Case under the care of Mr Rock Carling Epithelioma of dorsum and right lateral border of tongue, ulcerative type

Biopsy—Squamous-celled carcinoma No palpable cervical glands

Total Dose—1,716 mg hours

The condition before treatment is shown in Fig 13 The lesion healed entirely Six months later there was a small recurrence, this was again successfully irradiated Total dose, 528 mg hours The condition twelve months after treatment is shown in Fig 14

PLATE IV

Epithelioma of Tongue

- A Before treatment
- B Diagram to show depth of growth
- C Two months after treatment



A



B



C

The importance of this case is that it shows the possibility of applying radium more than once to the same portion of the tongue further, it shows that such application is successful and retrogression of the growth is obtained

Mr A P age sixty one years Under the care of Mr Arthur Evans and the author

Papillomatous growth on the under surface of the tongue and floor of mouth Enlarged cervical glands palpable in the right anterior and submaxillary triangle

Biopsy—Squamous celled carcinoma

Treatment—Ten needles at 0.6 mg of radium element each were inserted around the growth and left in position seven days

Total Dose—1,008 mg hours Entire disappearance of growth followed The neck was treated six weeks later by means of a collar carrying 40 mg of radium element in 1 foot fourteen hours daily for ten days Total dose 5,600 mg hour Entire disappearance of enlarged glands followed Well three years after

PALATE UVULA AND PILLARS OF FAUCES

Epitheliomata of the palate, uvula and pillars of the fauces cannot be easily cured by operation and radium treatment gives better results The prognosis for the primary growth is very good, and in a large proportion of cases the primary growth of the palate disappears on irradiation The ultimate prognosis is more grave owing to early and bilateral dissemination in the cervical gland Bilateral infection of the cervical lymphatics is more frequent in these situations than in any other form of interior cancer

Pillars of Fauces and Uvula Technique—The treatment of the primary growth of the pillars of the fauces and uvula is carried out by means of radon seeds In this situation seeds present many advantages After preliminary oral toilet, seeds are introduced by means of a trocar around and behind the growth, a regular distribution is aimed at the seeds being placed at a distance of 1 cm from each other With an initial strength of 1.8 or 2 M.C. per seed about eight to twelve seeds are necessary according to the extent of the lesion They are left in position for periods of seven to ten days, the patient is examined every second day and the seeds removed when there is evidence of reaction manifested by redness and slight oedema Hospitalist

tion is not essential, and the majority of these cases can be treated as out-patients at this stage. When seeds are used it is not necessary to provide for protection of the mandible by means of a lead-lined shield, as osteonecrosis is very unlikely to occur providing the seeds have 0.5 mm of platinum protection. If seeds are not available needles containing 0.6 mg of radium are used. They must be securely sutured in position, and this is facilitated by the use of cleft palate needles. Protection of the hard palate and of the lower jaw becomes necessary owing to the continuous maximum intensity during the whole period of treatment. The needles are left in position seven days, the average total is 1,000 mg hours.

Palate. Technique

There are three methods of irradiating the palate, and the choice is decided by the extent of the growth, the facilities for obtaining radon seeds and the services of a skilled dental mechanic.

Radon Seeds Method.—This is in every way similar to that used for the pillars of the fauces and uvula. It is useful in lesions of the palate of moderate extent and not involving the hard palate. The seeds are distributed equally around and in the growth and left in position seven to ten days.

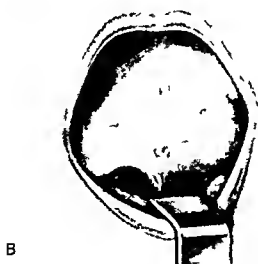
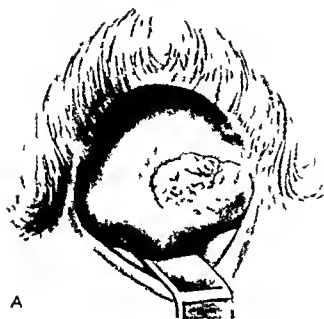
Needling.—Small needles of 0.6 mg each are inserted in the substance of the palate, care being taken not to perforate the soft palate or injure the underlying bone. There is no necessity for suturing the needles, but they are provided with a short thread for the purpose of withdrawal at the end of the treatment. The needles are kept in position by a lead-lined vulcanite plate fitting closely to the roof of the mouth and kept in position by the peripheral cup-like extension fitting over the alveolar margin (Fig 9, *a* and *b*). Protection of the lower jaw is not necessary. If difficulty is experienced in keeping the apparatus in position a cork is attached to one side of the plate, and this provides a point of purchase for the alveolus of the lower jaw. A bandage will keep the jaws in contact without undue fatigue to the patient.

PLATE V

Epithelioma of Palate

- A Condition before treatment
- B Condition five weeks after treatment

PLATE V





Intrabuccal Surface Application—This can be considered the method of choice, and is suitable for all cases except those involving the free border of the palate and the lips.

A plaster cast of the roof of the mouth and the lesion is taken. A vulcanite or stent apparatus is made and lined inside with 1.5 mm of lead, a window corresponding accurately to the extent of the lesion is cut in the upper surface of the plate, radium needles of 2, 1.3 and 0.6 mg are placed equidistally from each other and covered by vulcanite. Fifteen mg of radium are required. The plate is worn day and night for ten to fourteen days. It can be removed daily and the mouth irrigated with a mild antiseptic. At the end of five days the needles are rearranged so as to obtain a more uniform irradiation. The results are most satisfactory, and extensive carcinomata involving even the whole palate have been made to disappear. Care must be taken not to exceed 10 to 15 mg of radium and gamma irradiation only is to be used to prevent any possibility of necrosis. For the treatment of the glandular involvement of the neck, see Chapter V.

ILLUSTRATIVE CASE

Mr E. B. age seventy three years (Plate V)

Extensive epithelioma of palate ulcerative type. Large mass of glands on both sides of the neck.

Treatment—Eight needles at 0.6 mg. of radium element each for seven days. Total dose 734 mg. hours. Complete disappearance of growth.

The condition before and after treatment is shown in Plate V. Bilateral dissection of cervical glands was done followed by distant irradiation. 75 mg. of radium element in multiple foci applied on a Columbia paste collar sixteen hours daily for ten days. Total dose 13,000 mg. hours.

Enlargement of left supraclavicular glands twelve months later. Second radium collar total dose 25,000 mg. hours in twenty one days. Extensive peeling of the supraclavicular area. Disappearance of mass. Well eighteen months.

TONSIL

In this situation a distinction must be made between epithelioma and sarcoma. The latter is much more sensitive to irradiation and requires less irradiation.

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

26

27

28

29

30

31

32

33

34

35

36

37

38

39

40

41

42

43

44

45

46

47

48

49

50

51

52

53

54

55

56

57

58

59

60

61

62

63

64

65

66

67

68

69

70

71

72

73

74

75

76

77

78

79

80

81

82

83

84

85

86

87

88

89

90

91

92

93

94

95

96

97

98

99

100

101

102

103

104

105

106

107

108

109

110

111

112

113

114

115

116

117

118

119

120

121

122

123

124

125

126

127

128

129

130

131

132

133

134

135

136

137

138

139

140

141

142

143

144

145

146

147

148

149

150

151

152

153

154

155

156

157

158

159

160

161

162

163

164

165

166

167

168

169

170

171

172

173

174

175

176

177

178

179

180

181

182

183

184

185

186

187

188

189

190

191

192

193

194

195

196

197

198

199

200

201

202

203

204

205

206

207

208

209

210

211

212

213

214

215

216

217

218

219

220

221

222

223

224

225

226

227

228

229

230

231

232

233

234

235

236

237

238

239

240

241

242

243

244

245

246

247

248

249

250

251

252

253

254

255

256

257

258

259

260

261

262

263

264

265

266

267

268

269

270

271

272

273

274

275

276

277

278

279

280

281

282

283

284

285

286

287

288

289

290

291

292

293

294

295

296

297

298

299

300

301

302

303

304

305

306

307

308

309

310

311

312

313

314

315

316

317

318

319

320

321

322

323

324

325

326

327

328

329

330

331

332

333

334

335

336

337

338

339

340

341

342

343

344

345

346

347

348

349

350

351

352

353

354

355

356

357

358

359

360

361

362

363

364

365

366

367

368

369

370

371

372

373

374

375

376

377

378

379

380

381

382

383

384

385

386

387

388

389

390

391

392

393

394

395

396

397

398

399

400

401

402

403

404

405

406

407

408

409

410

411

412

413

414

415

416

417

418

419

420

421

422

423

424

425

426

427

428

429

430

431

432

433

434

435

436

437

438

439

440

441

442

443

444

445

446

447

448

449

450

451

452

453

454

455

456

457

458

459

460

461

462

463

464

465

466

467

468

469

470

471

472

473

474

475

476

477

478

479

480

481

482

483

484

485

486

487

488

489

490

491

492

493

494

495

496

497

498

499

500

501

502

503

504

505

506

507

508

509

510

511

512

513

514

515

516

517

518

519

520

521

522

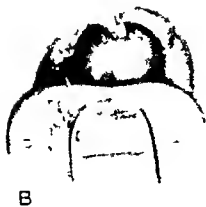
523

524

525

52

PLATE VI



done at this stage, as it is very important to disturb as little as possible the nutrition of the area treated

Second Stage—Immediately after the removal of the seeds or needles surface irradiation is carried out. A plaque of Columbia paste is moulded over the side of the face covering the lower jaw, the area of the operation and the upper part of the neck. Thirty mg of radium in multiple foci are distributed on the surface of the plaque and applied twelve hours daily for five to six days, a total dose of 2,000 to 3,000 mg hours being given. It is not advisable to give a bigger dose at this stage. For treatment of the cervical glands, see Chapter V.

ILLUSTRATIVE CASE

Mr G B age fifty three years (Plate VI) Epithelioma of right pillar of fauces involving tonsil and extending to free edge of palate and uvula. Duration three months. Palpable glands on right side of neck.

Treatment—Seven needles at 0.6 mg radium element each introduced and left in position seven days. Total dose 705 mg hours. Complete cicatrisation of lesion.

The condition before and after treatment is shown in Plate VI. One month after treatment of primary growth Crile's dissection performed. Glands found to be infected with secondary deposits. Five weeks later glands in left anterior triangle palpable. Dissection followed by immediate surface irradiation 25,000 mg hours in eighteen days.

Extensive peeling. Complete disappearance of mass. Well eight months.

BUCCAL MUCOSA

Epithelioma of the cheek responds well to radium treatment. The extent of the growth is the main factor in the choice of the technique adopted. Surface application from inside the mouth or externally may be used as an alternative to needling in this situation, and by this method there is less risk of perforation of the cheek and a more even distribution of radium is obtained. Needling with very small needles 9 mm long or seeds gives very good results.

Technique

For a localised growth not invading the muscles of the face or the gingival mucosa a stent, shellac or vulcanite

shield is made to fit either the lower or the upper jaw, whichever is most suitable for the individual case. A vertical plate is attached in the apparatus; this shield fits between the alveoli and the cheek and is in contact with the neoplasm (Figs 16, 17). It has an internal layer of 1.5 mm of lead

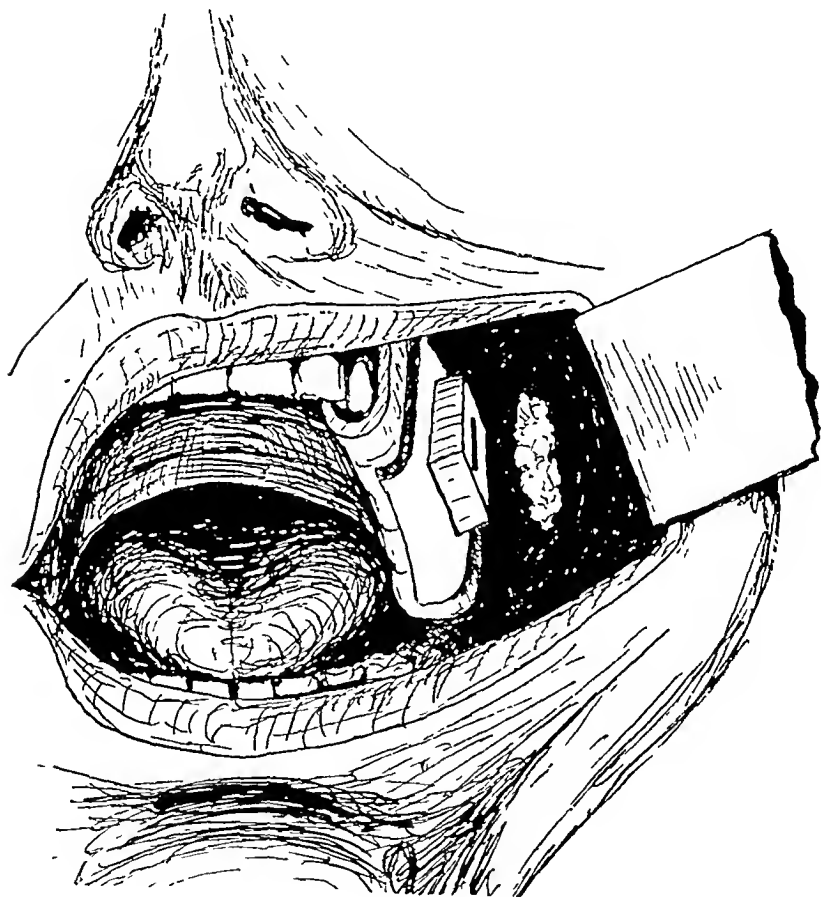


FIG 16

Intrabuccal apparatus lined with lead and carrying a small box containing radium. The box keeps the lesion and alveolar margins at a distance from the radium.

for protection of the alveoli. If space permits the vertical plate is replaced by a small flat box. Radium is placed in the box or on the lead and covered with vulcanite. The apparatus contains a total of 10 mg of radium, and is worn continuously for seven to ten days. A total dose of 2,000 to 3,000 mg hours is given.

If the growth has invaded the muscular layer of the cheek and there is difficulty in opening the mouth external application by means of a Columbia paste plaque is resorted to. The dosage in this case is increased to 5,000 mg hours. In cases of extension of the lesion to the gums the prognosis is

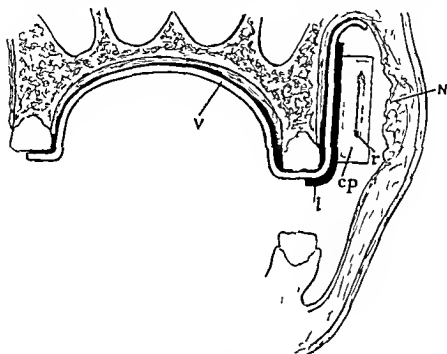


FIG 17

Diagram showing section of apparatus shown in Fig 16

v = vulcanite

l = lead

cp = Columbia paste

N = neoplasm

much worse, as there is a risk of osteo-necrosis from the irradiation

If needling is resorted to a total dose of 1,200 to 2,000 mg hours in seven to ten days is given by means of multiple small needles

ILLUSTRATIVE CASE

Mr O F age seventy four Under the care of Mr Arthur Evans and the author

Extensive ulcer of right cheek size of a five shilling piece

Biopsy —Squamous celled carcinoma Mass of glands in right submaxillary region

Treatment —Needling of growth with ten needles at 0.6 mg radium element each Left in position seven days

Total Dose—1,008 mg hours Complete disappearance of growth

Radium collar applied to neck but patient refused treatment after seven days' application

Mass of glands remained stationary for two years, then grew rapidly and fungated through the skin

Patient died two years after treatment At the time of death the mouth was normal

LIPS

Epitheliomata of the lip are treated by means of horse-shoe shaped Columbia paste plaques The growth is simultaneously irradiated from the inner and outer sides, 1 mm. of lead is used as a protection for the teeth and alveoli The dosage depends upon the size of the growth, 10 to 20 mg of radium are necessary in most cases The irradiation is intermittent, the patient being treated ten hours daily for two weeks The total dose varies from 1,400 to 3,000 mg. hours

ILLUSTRATIVE CASES

Mr J C A, age fifty-nine years (Plate VII) Under the care of Mr William Turner and the author

Epithelioma, nodular variety, of lip and buccal mucosa No enlarged cervical glands palpable

Treatment—Eight needles at 0.6 mg radium element each, introduced around the growth and left in position seven days Followed by surface application on wax for three days

Total Dose—1,200 mg hours Total disappearance of growth The condition before and after treatment is shown in Plate VII Well one year

Mr G G, age eighty-one years (Plate VIII) Under the care of Mr Arthur Evans

Epithelioma of angle of mouth, involving upper and lower lip No palpable cervical glands

Treatment—Eight needles at 0.6 mg radium element each, inserted around the growth and left in position seven days

Total Dose—820 mg hours Complete disappearance of growth The condition before and after treatment is shown in Plate VIII Well seven months

REFERENCES

- 40 HARMER, DOUGLAS W "Diathermy Operations for Cancer of the Tongue" *BJS*, 1928, Vol XV, No 60, p 661
- 41 QUICK, D "Radium in Treatment of Epithelioma of the Lip" *Journal of Radiology*, December, 1921

1885

1886

1887

1888

1889

1890 1891 1892 1893 1894 1895 1896 1897 1898 1899

PLATE VII

Epithelioma of Lip M^r William Turner's case

A Condition before treatment

B Condition two months after treatment



- 42 REGAUD CL Traitement des Cancers par Radium puncture
 Paris Med , 1920 Sur la Curietherapie des epithelomes de la
 langue et des adenopathies secondaire *Internat Cong Radiol*
 Lond , 1925 Paris Med October 1925
- 43 HARMER D Radium Treatment of Carcinoma of the Larynx and
 Tongue *St Bart's Hosp Report*, 1927 p 121
- 44 LEDOUX L Cancer de la Langue *Le Cancer*, 1924, No 3,
 p 20

CHAPTER V

CERVICAL LYMPHATIC GLANDS

THE late development of malignant deposits in the cervical glands long after the disappearance of the primary growth in the mouth and the systematic microscopical examination of all the glands excised show that there is a period of latency which may last eight to twelve months, during which ordinary clinical methods of examination cannot reveal the presence of malignant cervical deposits. The marked failures of incomplete operations for the removal of the cervical glands,⁴⁵ the hopelessness of cases where the glands are irremovable, and the death of patients from cervical deposits although the oral cavity is normal, are convincing proofs of the importance of early treatment. The problem presented by all cases is "What is the best possible treatment for the prevention or cure of lymphatic invasion by cancer?" The study of the ultimate fate of patients treated by operation, irradiation or a combination of methods and the experience gained from these cases which were not cured helps in the attempts to solve this problem. Is operative treatment preferable to irradiation? What can irradiation do in this situation? Is post-operative irradiation of value? Should irradiation precede operation? The answer to these questions depends upon many factors. The technique employed has been modified with increased experience and from experience of others, and from the collective experience of all the surgeons at Westminster Hospital the following conclusions were gradually arrived at

(1) Incomplete operation, viz, anything short of what is known as Crile's dissection, is by itself not to be recommended. Removal of the glands in the submaxillary triangle or along the main vascular sheath is not sufficient, and is followed in a large percentage of cases by local recurrence of the disease.

12 7 1 7 1 121
 1 122 22 7 1 121
 1 122 22 7 1 121

PLATE VIII

Epithelioma of Lip Mr Arthur Evans' case

A Condition before treatment

B Condition three months after treatment

PLATE VIII



A



B

(2) Incomplete operation, followed by insertion of radium in the wound, has been abandoned by most workers partly owing to the danger of inserting radium needles or tubes in the vicinity of big vessels, but chiefly to unsatisfactory results, as uniform irradiation is difficult, if not impossible, to achieve

(3) Incomplete operation, followed by surface irradiation with Columbia paste collars, has given better results, but cannot be said to be the ideal method of treatment

(4) Surface irradiation by means of Columbia paste collars alone has been successful in a certain number of cases, but there is no definite evidence that in these cases the glands were actually malignant. In other cases recurrences occurred after irradiation, this may be due to insufficient dosage

(5) Extensive dissection of the cervical fascia and lymphatics on the lines advocated by Crile has given good results, but is by itself considered as insufficient if malignant glands are present, and is not indicated if malignant glands are not present

On the clinical side the following points must be considered —

(1) Does absence of palpable glands offer a certain indication of freedom from disease? In a number of cases the primary lesion was completely cured and remained cured. No palpable glands were detected in the neck for several months after the disappearance of the primary growth and then developed rapidly. In one case of epithelioma on the side of the tongue this occurred twelve months after treatment of the primary growth and led to a fatal issue in spite of treatment. In another patient secondary deposits in the neck appeared two and a half years after successful treatment of a laryngeal carcinoma

(2) Not all enlarged glands are necessarily malignant. Systematic examination of all the glands removed has shown this repeatedly

(3) What can be achieved by treatment in cases of (a) operable glands, (b) inoperable glands

(4) The general health of the patient must be considered. Limitations of active treatment imposed by cardio-vascular or pulmonary lesions, obesity, metabolic disease, etc.,



FIG 18

Photomicrograph (magnified 95 diameters) showing a deposit of a squamous-celled carcinoma in a lymphatic gland. The section also shows periadenitis and permeation of lymphoid tissue by œdema fluid (Histology by Dr Braxton Hicks)

must guide the treatment. Palliative measures such as moderate irradiation are to be given preference to masterly inactivity

Pathology of Enlarged Glands

In a series of over thirty cases a complete dissection of all the lymphatic glands in the neck was done. On six occa-

sions a bilateral operation was performed. The glands were dissected out from the mass removed and histological sections of each gland individually examined by Dr. Hicks.



Photomicrograph (H&E) of
marked irritation. All the
medulla is completely filled
lymphoid tissue in the
cells (H&E, 100x, D. H.)

Hicks. The result of the operation was that the glands can be classified into three groups:

- (a) Infected with epithelioma
- (b) A stage of irritation in which the follicles in the gland are being replaced by lymphoid cells
- (c) A stage of hyperplasia

These stages are quite distinct, as can be seen from the photomicrographs. They are found in the examination of axillary glands in cases of mammary cancer. They can



FIG 20

Photomicrograph (magnified 95 diameters) showing the earliest changes observed in the lymphatic glands draining an area of cancer. The condition is one of hyperplasia, the normal structures seen in a lymphatic gland being accentuated. The section shows the prominence of the lymphoid nodules of the cortex and the general cellularity of the rest of the lymphatic gland. (Histology by Dr Braxton Hicks.)

be considered as precancerous, and if left untreated will become typical secondary deposits.

From the foregoing considerations the following scheme of treatment was evolved. It presents certain advantages of classification and uniformity of treatment, it has given

relatively satisfactory results which are being improved as time goes on. The ultimate treatment will be modified with improvement of technique of radium therapy, with the acquisition of larger quantities of radium permitting distance irradiation and possibly by combination of irradiation with some form of chemo- or actino-therapy.

Unpalpable Glands

In cases of cancer of the lip and buccal mucosa if no palpable glands are present no active treatment is indicated. Observation of the patient at regular intervals is sufficient. In cases of cancer of the tongue floor of the mouth palate fauces and tonsil the following treatment is carried out.

First Stage—Irradiation of the primary growth (see Chapter IV)

Second Stage—A month after irradiation of the primary lesion operative removal of the glands on the side of the lesion is carried out.

Operation—The operation must aim at the eradication of all the glands the deep fascia sterno-mastoid muscle and internal jugular vein following Crile's technique. The removal of the sterno-mastoid simplifies the operation and gives a much better exposure of the glandular area. According to the situation of the primary growth particular attention will be paid to certain areas of the neck. Thus, if the primary growth is on the floor of the mouth or inferior part of the tongue there is as a rule involvement of the submental and submaxillary glands. If the growth is situated in the antero-lateral aspect of the tongue the submaxillary and carotid groups of glands are frequently affected and the submaxillary group on the opposite side is frequently affected. In the postero-dorsal situation the submaxillary glands are usually involved first and in some cases the only glands implicated.

The study of the correlation between the primary growth and the lymphatic involvement and the distribution of the primary deposits shows their wide but not indeterminate distribution. It also shows the necessity of a

operation The removal of the internal jugular vein with all adjacent glands should be carried out from just above the clavicle up to the base of the skull or as near it as practicable The posterior belly of the digastric should be denuded of all fascia, and the angle and the inferior border of the mandible must be exposed. The deep fascia is removed up to the middle line of the neck At the end of the operation the suprahyoid, infrahyoid and scalene muscles must be denuded of all fascia. For several days after the operation some œdema of the lower half of the face is present. Temporary lower facial palsy is also unavoidable, but disappears in a few weeks

For a short period of time the patient experiences some difficulty in fully opening the mouth When the operation is carried out under regional anæsthesia combined with preliminary administration of paraldehyde per rectum, the general condition of the patient is only slightly affected, and recovery is rapid

All glands removed must be individually examined histologically, and only in the absence of any deposits is no further treatment indicated

If one gland or more show secondary deposits the neck must be irradiated as described under the following group

Palpable Glands

The treatment will consist of —

First Stage.—Treatment of primary growth

Second Stage.—Operative removal of glands as described above A bilateral dissection is called for if there are palpable glands on both sides, and in cases where the primary lesion has transgressed the middle line In these circumstances it is advisable to allow an interval of a week between the two operations, and obviously the internal jugular vein must only be removed on the most affected side There is no disability after a bilateral removal of the sterno-mastoid muscles

Third Stage.—The third stage of the treatment is carried out three to four weeks after the operation The wound

by then is soundly healed. A collar of Columbia paste of 15 mm thickness is made. The collar embraces both sides of the neck (Fig 21). An average of 70 mg of radium is necessary. It is best to use needles of 1.3 or 2 mg each. The operated side receives one-third and the non-operated side two-thirds of the total quantity of radium. The average period of treatment is two weeks, the treatment is intermittent and the patient receives sixteen hours daily.



FIG 21—COLUMBIA PASTE COLLAR FOR THE TREATMENT OF THE CERVICAL AREA

The collar is 15 mm thick and is in contact with the skin in the submaxillary and carotid areas but fits loosely over the clavicles. The radium needles (not shown) are applied on the surface and the whole area is covered with adhesive plaster.

The total post-operative dose is 10 000 mg hours. It must be understood that this figure is not correct from the point of view of physics. It is the dose emitted by the apparatus, but not the dose received by the patient. There is also the factor that the radium is on both sides of the neck and some structures are irradiated from both sides simultaneously. The figure obtained is nevertheless useful for the purpose of notation and comparison erythema or superficial desquamation being the objective signs of sufficient irradiation.

ILLUSTRATIVE CASES

Mr A C G , age sixty years Under the care of Mr Arthur Evans and the author

Epithelioma of the left lateral border of the tongue Six weeks' history No enlarged palpable glands Successful radium treatment of primary lesion Two months after treatment a small gland was palpable behind the angle of the jaw on the left side , this



FIG 22

Photomicrograph (magnified 9 diameters) of cervical lymphatic gland with secondary deposit of squamous-celled carcinoma from lingual cancer

increased in size and a second larger gland appeared at the level of the bifurcation of the carotid The glands were excised and showed secondary deposits of squamous-celled carcinoma (Figs 22 and 23)

Post-operative irradiation by means of a Columbia paste collar was given Total dose, 15,000 mg hours Clinically well four years

Mr. P E , age forty years Under the care of Mr Gilbert Chubb and the author Extensive carcinoma of arytenoids and vocal cords Palpable hard glands both sides of the neck Total

laryngectomy performed Glands not removed Post operative irradiation by Columbia paste collar Total dose 17,000 mg hours Disappearance of glands Well two and half years

Mrs H, age forty years Post cricoid carcinoma with mass of inoperable glands on left side of the neck Laryngopharyngectomy performed Post operative irradiation with Columbia paste collar, 12,000 mg hours Disappearance of mass Well two years



FIG. 23

The same as Fig. 18 magnified 300 diameters

Mr J. C. age fifty three years Under the care of Mr. Rock Carling

Epithelioma of the floor of mouth ulcerative type successfully treated by radium

Wide dissection of malignant cervical glands followed by post operative surface irradiation with Columbia paste collar Well three years

TREATMENT OF INOPERABLE CASES⁴

In cases where the mass of glands is fixed and involves the cellular tissues of the neck complete surgical removal is impossible and radium therapy presents the only possible

means of alleviating the patient. No case, however extensive the glandular involvement, should be left untreated. Where the mass in the neck is of considerable size but movable, an attempt at removal is justifiable, this procedure, which at first appears most unsurgical, is done in order to diminish the total mass to be irradiated and to lessen the general reaction. Operation is followed by immediate irradiation by means of a Columbia paste collar. Bilateral irradiation is inadvisable in this group of cases. The reaction aimed at is severe and consists in complete peeling of the skin (Plate IX.). It is important to irradiate the mass very slowly, and at least three weeks' treatment is advised. The amount of radium varies with the size of the mass to be destroyed. Twenty to twenty-three hours daily are given. The total dose given amounts to 25,000 to 30,000 mg. hours. By this method good results are obtained in cases where no other form of treatment is possible. As to permanency of these results, all that can be said at present is that patients have remained well up till two years after treatment, and when it is noted that these patients had large masses of glands, and were inoperable, the results are very encouraging (Plates IX and XII.)

It may be argued that if such results are possible with inoperable cases, why not adopt this method in early cases and dispense with operation altogether? In the present state of radium therapy, the results are not sufficiently constant to justify this, and although palliation of symptoms and prolongation of life are obtained in inoperable cases, a combination of surgery and irradiation is still the best policy in operable cases.

ILLUSTRATIVE CASES

Mr J H W, age fifty (Plate IX) Epithelioma of upper lip excised in a hospital in the south of England. Rapid local recurrence with masses of secondary deposits on both sides of the neck. Columbia paste collar applied to face and both sides of the neck.

Total dose, 30,000 mg. hours in twenty-three days. Disappearance of malignant glands. Skin healed in five weeks.

Death from secondary deposits in the brain.

[illegible]

PLATE IX

Extensive peeling following irradiation of neck and face for recurrence of epithelioma of the lip and masses of fixed malignant cervical glands. The total dose given was 30,000 mg. hours in twenty-three days. The drawing was made four days after cessation of treatment. The area healed in about five weeks. Patient died ultimately from secondary deposits in the brain.

PLATE IX.



PLATE IX.

Mr K W age sixty Inoperable mass of hard glands in left anterior triangle of the neck No primary lesion detected

Biopsy —Primary carcinoma of lymphatic glands Surface irradiation with Columbia paste collar

Total dose 20 000 mg hours Extensive peeling Healed in five weeks Complete disappearance of mass Well two years

Mr T Alek age sixty Extensive and inoperable carcinoma involving two thirds of the tongue Radium treatment followed by glossectomy with diathermy Inoperable masses of glands on both sides of neck Columbia paste collar

Total dose 40 000 mg hours Disappearance of masses in the neck Survival of fourteen months death from secondary deposits in liver

Mr W J K age seventy six Extensive epithelioma of arytenoids and vocal cords Total laryngectomy Mass of malignant glands firmly adherent to bifurcation of right carotid Columbia paste collar

Total dose 20 000 mg hours Extensive peeling Disappearance of mass for three and a half years

REFERENCES

- 45 ROLX BERGER J I Le Curage des ganglions du Cou *Press Med* No 36 19-7
- 46 CADRE S and BRAXTON HICKS J A The Application of a Knowledge of the Lymphatic Drainage in Cancer of the Tongue and Mouth and the Importance of Prophylactic Irradiation in these Cases *Ann Rep Brit Emp Canc Camp* 1927-28 p 63
- 47 CADRE S The Radium Treatment of Cancer of the Buccal Cavity *Rep Intern Conferen Cancer Lond* 1928 pp 153-161

CHAPTER VI

PHARYNX AND LARYNX

EPITHELIOMATA of the pharynx and larynx form a group of neoplasms which if operable necessitates wide excision and severe mutilation of the patient. Every attempt to substitute excision by irradiation is justifiable, even if the percentage of results of the latter method of treatment are no better than those of the former. In growths of the vocal cords the functional results obtained by radium therapy are strikingly better than those obtained by laryngo-fissure.

Radium treatment of these types of tumour demands a precise knowledge of the local situation and extent of the growth. The time-honoured classification of laryngeal cancers into extrinsic and intrinsic is too indefinite and arbitrary, as extrinsic carcinoma is often, in fact, a lateral pharyngeal growth.

It is preferable to subdivide the growths of these situations in the following groups.

(1) **Endolaryngeal Tumours.**—These comprise tumours of the vocal cords, ventricular bands and anterior commissure, they are the least malignant group. Probably there is no form of cancer in the body in which such a high percentage of cures can be obtained almost by any form of surgical treatment.

(2) **Epilaryngeal Tumours.**—These are epitheliomata of the arytenoid region, they extend to the aryepiglottic folds and invade the epiglottis.

(3) **Lateral Pharyngeal Tumours.**—They are the epitheliomata of the sinus pyriformis and invade the lateral wall of the pharynx as well as the thyroid cartilage.

(4) **Hypopharyngeal Tumours.**—These include the "post cricoid" carcinoma and epitheliomata of the posterior wall of the pharynx.

The methods of treatment by means of radium vary with the situation. Before deciding on the line of treatment in endoscopic examination is made. The object of the examination is to ascertain the exact position and extent of the growth, and in some cases, when thought desirable to excise a small portion for histological examination. In view of the difficulty of early diagnosis in some cases this step is justifiable, although it may not be completely devoid of risk unless the tumour is irradiated at the same time. Further microscopic sections in these situations are often misleading. Valuable time is lost only too frequently in periods of observation in the hope that the lesion may not be malignant. A positive Wassermann reaction is of as little value here as in cases of cancer of the tongue. A positive Wassermann reaction is no evidence of presence or absence of malignant disease and no time should be lost in anti-syphilitic treatment. It is important in all cases of laryngeal and pharyngeal carcinoma to eliminate all sepsis in the mouth before beginning the treatment. All carious or even suspected teeth should be extracted before irradiation. Numerous methods of radium treatment have been advocated in the treatment of this group of malignant disease. It is unnecessary to pass in review the various forms of technique which have become obsolete, but special mention must be made of the introduction of large quantities of radium *per vias naturalis* only to condemn it as dangerous and unsatisfactory. The methods described are those which have in practice given sufficiently good results to recommend their use as a substitute for excision.

ENDOLARYNGEAL TUMOURS

These tumours manifest themselves early by hoarseness, they are of slow growth and do not tend to invade the skeleton of the larynx till the disease is very advanced. They do not, as a rule, give rise to secondary deposits in the cervical lymphatics. They are amenable to treatment by laryngo-fissure with a very good percentage of recovery. Radium treatment, however, is superior as it leaves the

patient with a much better voice, at times indistinguishable from normal

The method of treatment is based on the technique of Ledoux ⁴⁸ It has been practised by Harmer and Finzi ⁴⁹ with remarkable success even in operable cases. A gramophone record demonstrating the voice of patients treated by them was exhibited by Finzi ⁴⁹ at the International Congress of Radiology in Stockholm in 1928 and showed the possibilities of this method of treatment and the good functional results obtained

Technique of the Fenestration Method

The following is the operative technique as described by Harmer ⁵⁰ (Fig 24)

“ A skin incision is made over the thyroid cartilage, starting at the centre of the hyoid bone and extending outwards and downwards along the posterior border of the thyroid cartilage The infrahyoid muscles are exposed and split longitudinally The lateral aspect of the thyroid cartilage is exposed The perichondrium covering it is divided and stripped backwards and forwards The greater part of the cartilage is then resected Thus a large window is made in the thyroid cartilage, but a framework is left consisting of the four margins By this means the outer surface of the growth covered by the perichondrium is exposed It is important not to destroy this capsule or to cut into the growth The cartilage is removed for two reasons—to allow the needles to be placed as close to the growth as possible, and to prevent the perichondritis or necrosis which may be caused by radium

“ From five to ten radium needles are thus inserted lying parallel to one another and vertical To keep them in position the ends of the needles are tucked under the framework of the cartilage Care is taken that the needles do not penetrate into the growth or into the larynx At the lower end of the wound, if the growth is sub-glottic, the needles are pushed inside the cricoid ring, but in this situation the tissues are often so thin that occasionally the needles may perforate the air-passages Each needle has attached to it a piece of linen thread soaked in a solution of flavine 1/1,000 This material seems to cause less irritation than silk or others that have been tried The threads are tied together and buried beneath the muscles Double sutures are inserted into the skin, half of them being tied at once to close the wound completely and the other half left so that they can be tied later, after the radium has been removed No drainage is employed and the skin incision is completely sealed with a collodion dressing If the growth has extended across the

middle line a second window is made in the thyroid cartilage on the opposite side, and needles are buried there also. A low tracheotomy is then performed. This is deliberately made the last stage of the operation to prevent infection of the laryngeal wound. Tracheotomy has been performed in all the cases because the reaction which results from the radium may cause so much swelling that the glottis may become temporarily obstructed.

The operation is done either under regional anaesthesia or intratracheal intubation. The needles employed contain

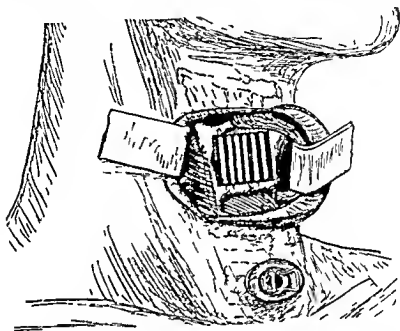


FIG. 4.—FENESTRATION OPERATION

A window has been cut in the thyroid cartilage and the radium needles are shown in position.

13 mg. of radium, and are left in position seven days. Seven needles are necessary as a rule, and the average total dose given is 1,600 mg. hours.

EPILARYNGEAL TUMOURS

This group of tumours consists of epitheliomata of the epiglottis, aryepiglottic folds and arytenoids. It presents itself in the form of an ulcerated or cauliflower variety and is always infected. It invades cartilage at an early stage and gives rise to secondary lymphatic invasion. The group of glands most frequently affected is the upper jugular

Transient pain, slight dysphagia and cough are the clinical manifestations.

Treatment

First Stage.—Preliminary tracheotomy is seldom necessary, if it is done the tracheotomy tube should be made of rubber or vulcanite to avoid secondary irradiations. Irradiation of the primary growth is done by direct laryngoscopy with platinum radon seeds of 1·8 to 2 M C initial strength. The seeds are implanted into and around the tumour and left in position for ten to fourteen days. Their removal necessitates an anæsthetic either local or general. The tracheotomy tube is removed three days after the removal of the seeds.

Second Stage.—Three weeks after irradiation excision of the cervical glands on the side affected is done. It is occasionally necessary to do a bilateral dissection.

Third Stage.—Surface irradiation by means of a Columbia paste collar 15 mm thick. The collar surrounds the neck, and the suprahyoid, submaxillary and carotid areas are irradiated, 70 mg of radium are required. The application is *intermittent of eighteen hours daily for a period of two to three weeks*. Total dose, 18,000 to 25,000 mg hours.

LATERAL PHARYNGEAL TUMOURS

These are tumours of the pyriform fossa. They are clinically silent and lead to rapid and early lymphatic dissemination. In these growths secondary deposits in the neck predominate in the clinical picture. They are, as a rule, inoperable when first seen. Surgical treatment, as advocated by Wilfred Trotter,⁵¹ consists in a pharyngolaryngectomy. Cure by surgical means is possible but exceptional, and so the gravity of this condition cannot be overestimated. Radium treatment in this situation does not give as good results as in other situations of this group. It presents, however, the advantage of being applicable to all cases, operable or inoperable. It gives good palliative results, and prolongs life in comfort without the ordeal of a tracheotomy, a pharyngeal fistula or gastrostomy.

Technique

In this situation both the primary growth and the cervical lymphatics are treated simultaneously. Surface irradiation by Columbia paste collars is employed. Both sides of the neck are irradiated at the same time, 100 mg of radium in numerous small needles are necessary. They are distributed on both sides of the neck, a sheet of lead 1 mm thick is used to protect the thyroid cartilage. Treatment is prolonged to three weeks, the patient receiving sixteen hours daily. The average total dose given is over 30,000 mg hours. The reaction is severe. The mucosa of the mouth and pharynx become dry and red. There is marked hoarseness towards the end of the treatment and some œdema of the glottis. Peeling of the skin is extensive. The acute laryngeal reaction subsides in one week, but loss of voice may persist for four to six weeks. The immediate results are good, and patients can be kept in comfort for two or three years. Recurrence, however, is frequent.

HYPOPHARYNGEAL TUMOURS

These tumours occupy the anterior or posterior wall of the pharynx. They are spoken of in the first case as 'post-cricoid carcinoma,' but extend at a variable distance into the pharynx.

They cause dysphagia and give rise to rapid dissemination. The extent of the growth is very difficult to estimate clinically, even on endoscopic examination under anaesthesia. The disease is rapidly fatal and lends itself badly to surgical removal.

Early cases are extremely rare and there is great difficulty in obtaining access to them, of all surgical procedures Trotter's operation⁵¹ probably gives the best results. Inoperable cases are the rule, and in these it is often difficult to decide whether any treatment is advisable. The answer depends upon the general condition of the patient.

Intensive X-ray treatment, carried out by an expert with special experience of this type of case, gives at times very good palliative results.

Treatment

First Stage.—It is important to carry out the treatment under local or regional anæsthesia, as the risk of post-

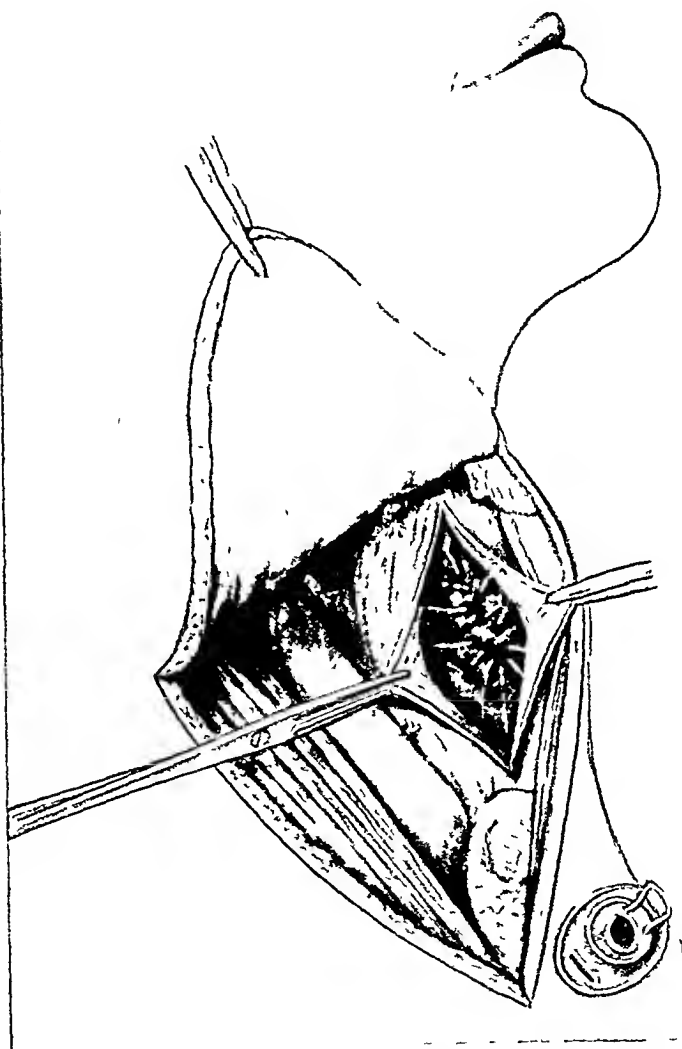


FIG 25 —EPITHELIOMA OF LEFT LATERAL PHARYNGEAL WALL

A right lateral pharyngotomy has been performed. Portions of the hyoid bone and thyroid cartilage have been resected. The superior thyroid artery and common facial vein have been divided between ligatures. The pharynx is incised. Twelve seeds are shown half introduced into and around the growth.

anæsthetic pneumonia is great. Preliminary tracheotomy is performed. The interior of the pharynx is exposed by lateral pharyngotomy on the sound side (Fig 25). Platinum

radon seeds of 1.8 M.C. initial strength are introduced into and around the growth. The seeds are not provided with threads, as their removal is not anticipated. The pharynx is closed by a double layer of sutures. Nasal feeding is resorted to for the first fourteen days. Operative removal of the glands is inadvisable. The pharynx is opened on the sound side for the following reasons: (1) to avoid cutting into the growth, (2) to avoid disturbance of the lymphatic area, (3) to facilitate closure of the wound.

Second Stage—Four weeks after irradiation the whole neck is treated by a Columbia paste collar. The total dose given is 20,000 mg. hours in sixteen days.

ILLUSTRATIVE CASES

Mr R. F. age sixty years. Carcinoma of left pyriform fossa with mass of glands the size of a pigeon's egg behind the angle of jaw.

Biopsy—Squamous celled carcinoma. Columbia paste collar applied.

Total dose, 16,000 mg. hours in twelve days. Extensive peeling. Disappearance of mass of glands and of primary growth. Well, eighteen months.

Mr S. S. G. age fifty three. Extensive malignant disease involving right epiglottic area, upper part of pharynx and lateral wall of pharynx. Palpable hard glands left and right sides of neck.

Treatment—(1) Fenestration operation, six needles at 1.3 mg. radium element for seven days. Total dose 1,330 mg. hours. (2) Radium collar, 75 mg. eighteen hours daily for nineteen days. Total dose 25,650 mg. hours. Recovery of voice. Disappearance of primary growth. Partial disappearance of cervical glands. Indefinite thickening palpable on right side of neck. General health good. Well sixteen months.

REFERENCES

- 48 LEDOUX I. La radio et radiumthérapie en oto-rhino-laryngologie. *Journal Belge de Radiologie* 1923 Vol. VII fasc. 2 p. 60.
- 49 FINZI N. S. and HARMER D. Radium Treatment of Intrinsic Carcinoma of the Larynx. *B. M. J.* November 17th 1928 p. 886.
- 50 HARMER D. Radium Treatment of Carcinoma of Larynx and Tongue. *St. Bart's Hosp. Report* 1927 p. 113.
- 51 TROTTER W. Operations for Malignant Disease of the Oral and Laryngeal parts of the Pharynx. Burghard's System of Operative Surgery, 2nd edition Vol. II pp. 260-263 and Operative Treatment of Malignant Disease of the Mouth and Pharynx. *The Lancet* April 19th 1913 p. 1.

CHAPTER VII

CARCINOMA OF THE BREAST

THE prognosis in cancer of the breast treated by the modern extensive operation (modified Halstead) depends upon the following factors :

(1) Age of the patient , (2) Type of growth , (3) Extent of disease , (4) Presence of pregnancy or lactation

In an attempt to assess the prognosis, survival of five years after operation is considered as the basis—this period of time being spoken of as “cure” To arrive at an estimate of prognosis the surgeon relies upon his experience, statistics and an element of luck, the “unknown factor” which plays a part, inasmuch as cases apparently hopeless are occasionally cured Modern surgical teaching lays stress on the importance of an extensive operation, wide removal of fascia, careful dissection of the axilla These various points are relied upon to save the patient from recurrence, providing the disease is local, or at least localised to the territory covered by the operation If the disease has spread beyond these limits surgery is powerless, and is employed as a palliative measure only In considering the end results of extensive operation, it is seen that recurrence takes place in the following situations

- (1) Vicinity of the scar
- (2) Supraclavicular glands
- (3) Mediastinum, pleura, lungs.
- (4) Bones

The lesson to be learned from the study of the distribution of these recurrences and of the times at which they occur is twofold

(1) However extensive the operation, it is not extensive enough to carry the surgical act beyond the limits of the disease

(2) That recurrences may take a long time to appear, and therefore it must be assumed that they have been present all the time, but were inactive, and that their presence cannot be recognised clinically

No comparison of the relative value of surgery and irradiation is attempted in these pages. Advantages such as the relative percentage of operative mortality of each method are of no importance if the end results of the method with a trivial operative mortality are bad as compared to the other. Comparison of the two methods is only considered from the point of view of ultimate cure, and for this the essential factor, time, is at present not yet available for radium therapy. The possibility of radium therapy, however, has been very well demonstrated in the treatment of advanced and inoperable cases and in the treatment of post-operative recurrence.

The consideration of these cases demonstrates the possibility of making large masses of cancer disappear by radium. The possibility of apparent cures of cancer of the breast by radium has been demonstrated by De Nabias,⁵² Geoffrey Keynes,⁵³ and others. In the museum of the Westminster Hospital Medical School are preserved several specimens of breasts treated by radium and amputated several months after cessation of treatment—these specimens show no evidence of malignant disease either macro- or microscopically, although they were typical cases of carcinoma "en cuirasse" when the patients first came for treatment. Similar results were obtained by Roy Ward⁵⁴ at the Radium Institute, London, Burton Lee,⁵⁵ in New York and others.

If radium treatment is capable of destroying large masses of breast carcinoma, involving adjacent tissues, it is equally capable of dealing with small masses in the operable stage. The great advantage of radium, however, lies in the fact that it can be extended beyond the field covered by surgery. The methods employed at Westminster Hospital have been gradually progressive. At first surface application alone was used, in other cases needling, finally a combination of both methods. From the experience gained a technique

was evolved which is applicable to the majority of cases, operable or inoperable. It aims at a "Radium Halstead," and, in fact, extends over a much wider area than that covered by the most extensive operation.

Biopsy

Up till recently all cases of cancer of the breast treated by radium were submitted to a preliminary biopsy, either from the primary growth, a cutaneous nodule or a lymphatic gland. This was considered an essential step, as it was necessary to establish beyond doubt a proof, which was also a permanent record, of the malignant nature of the lesion treated. When the effect of radium on carcinoma had been proved in a series of cases, and it became a recognised fact that radium could destroy malignant growths, the practice of a preliminary biopsy was abandoned. A biopsy is not necessary to "preach to the converted", it is of no value to the patient if the surgeon is satisfied clinically as to the nature of the lesion, it is not practised as a routine when surgical treatment alone is adopted, and it is no more justifiable to do a biopsy for the sole reason of providing evidence for those who remain blind to the possibilities of radium treatment.

Treatment

Radium treatment of cancer of the breast comprises two stages. A first stage of interstitial irradiation, followed a month later by surface treatment.

First Stage.—The first stage consists in the introduction of suitable radium needles into and around the primary growth, along the periphery of the breast, in the axilla, the intercostal spaces, above and below the clavicle and along the midaxillary line (Fig. 26).

Technique

The insertion of needles is carried out under local anæsthesia, with preliminary administration of paraldehyde per rectum. Local anæsthesia consists in the intro-

duction of $\frac{1}{2}$ per cent novocain into the skin, forming dermal wheals and infiltration of the track along which the radium

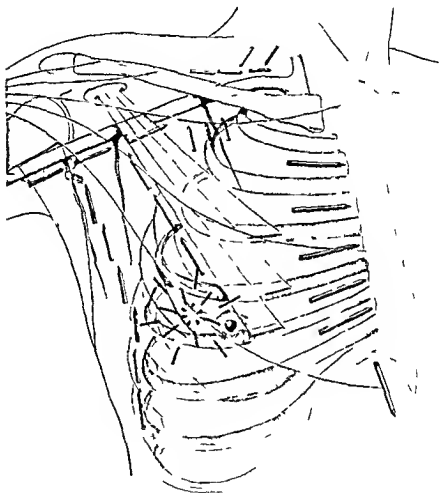


FIG. 6

Scheme of distribution of needles in the treatment of cancer of the breast. It shows the needles:

- (1) in the tumour
- (2) around the tumour
- (3) in the parasternal area
- (4) along the costo-coracoid membrane
- (5) in the supraclavicular area
- (6) in the axilla
- (7) in the midaxillary line

needle is to be introduced. It is done by the assistant immediately previous to the introduction of each radium

needle. The skin is not incised as the needles have trocar points, and by avoiding incision less sepsis follows the treatment. The needles are threaded with white thread, soaked in flavin, tied and knotted at the eye, one strand is cut short, the other carries a china or glass bead of a distinctive colour allotted to indicate the strength of each of the various needles used. There is no necessity to suture the needles in position. They must be completely buried. Needling is carried out with the same strict aseptic precautions as any other surgical procedure. The number of needles depends upon the size of the tumour and the size of the breast to be treated.

DISTRIBUTION OF THE NEEDLES

(1) **Tumour.**—Needles containing 0.5 mg. of radium screened by 0.5 mm. of platinum, 9 mm. long, are inserted into the tumour at a distance of $\frac{1}{2}$ inch from each other.

(2) **Periphery of Tumour.**—Needles of 1 mg. of radium, 0.8 mm. of platinum, 24.5 mm. long are inserted around the tumour at a distance of 1 cm. from each other. They form a corona surrounding the growth, and are introduced in such a way that the whole needle is in the substance of the breast. Two circles are necessary to irradiate a large breast.

(3) **Parasternal Area.**—Needles of 1.5 mg. of radium, 1 mm. of platinum, 30 mm. long, are introduced horizontally from the periphery towards the sternum into each of the upper four intercostal spaces.

(4) **Costocoracoid Membrane.**—Needles of 2 mg. of radium, 0.65 mm. of platinum, 33 mm. long, are introduced vertically at 1 cm. from each other below the clavicle and deep to the pectoralis major. The trocar points are directed upwards towards the clavicle.

(5) **Supraclavicular Area.**—2 mg. needles are inserted horizontally above the clavicle, deep to the deep fascia and sterno-mastoid, they extend along the clavicle and into the posterior triangle of the neck.

(6) **Axilla.**—2 mg. and 1.3 mg. needles are used to

irradiate the axilla This is done systematically—(a) along the axillary border of the pectoralis major, (b) along the main vessels, (c) in the apex of the axilla

(7) Midaxillary Line—Needles containing 2 mg of radium each are inserted posterior to the breast from the axilla downwards forming a barrage along the serratus magnus

In all about forty to fifty needles containing 75 to 100 mg of radium are inserted The threads are arranged on the surface of the skin, and the punctures and threads are painted with collodion A dressing of gauze and wool is applied The introduction of the needles causes no shock, and the primary mortality should be *nil* The dressing is not disturbed till the third day The area treated is inspected every third day The needles are removed on the ninth day The average total dose administered varies between 16,000 and 21,000 mg hours There is invariably some sepsis at the site of the punctures when the needles are removed It is never severe, and subsides in three to four days with hot fomentations The patient is fit to be discharged from the hospital fourteen days after the admission

Condition after Treatment—There is some œdema of the skin and subcutaneous tissues, the primary tumour is very much softer, smaller, and its borders are not sharply defined, but merge imperceptibly into the surrounding breast tissue The movements of the arm are unaffected The general health of the patient does not suffer from the treatment (Figs 27 and 28)

The patient is examined at weekly intervals, and re-admitted to hospital four or five weeks later

Second Stage—A Columbia paste cast 15 mm thick is made It covers the lower half of the neck and the anterior and lateral parts of the chest extending to the costal margin in front One mm of lead is placed over the clavicle, the sternum and over the spleen or liver according to the side treated (Fig 29)

A second Columbia paste cast is made for the back,

extending from above the scapula down to the ninth rib and the posterolateral aspect of the chest

A total of 75 to 100 mg of radium in numerous needles of 2 mg., 1.3 mg., 1 mg., 0.6 mg. is distributed equally over the whole of the cast. The needles are placed between two layers of adhesive plaster, and this is applied to the surface of the wax plaque. The anterior and posterior



FIG. 27.—APPEARANCE OF BREAST AFTER REMOVAL OF NEEDLES
The needle punctures are plainly visible. The tumour has disappeared.
There is some œdema of the area treated.

aspects of the chest are irradiated alternately, the adhesive plaster containing the radium needles being transferred from one to the other. Irradiation is continuous, the patient receiving twelve hours anteriorly and twelve hours posteriorly. The treatment is continued for fourteen days, the average total dose being 35,000 mg. hours in equal halves for each aspect of the thorax.

This extensive irradiation aims at the sterilisation of the cells which have not been affected by the needling, and to

provide for the irradiation of the mediastinum, pleura and lungs. The total dose received intrathoracically is high, but as there are three ports of entry (anterior, posterior and lateral) the skin is only slightly affected. Pigmentation of



FIG 28

Skigram showing distribution of radium needles in case of patient in Fig 27. The small circular shadows are the beads attached to the distal end of the threads for identification purposes.

the skin follows as a rule, but peeling is very exceptional. The advantage of a two stage treatment is that peeling is avoided, convalescence is shortened, a period of rest is given to the patient and the treatment seems to be more efficient.

Right Breast — Pig skin over the whole breast, in the centre is a hard mass adherent to chest wall the breast is completely fixed to parietes Palpable glands in right axilla

Left Breast — Tumour palpable and visible above the nipple adherent to skin and to fascia breast fixed to parietes Enlarged glands palpable in left axilla

Treatment — Simultaneous irradiation of both breasts and both axillæ

Interstitial Irradiation — Right breast 786 mg in 23 foci ten days Total dose 18 864 mg hours Left breast 423 mg hours in 18 foci for ten days Total dose 10,152 mg hours

Surface Irradiation — Right breast 1,440 mg hours left breast, 4 560 mg hours

The general health of the patient improved as can be seen from the

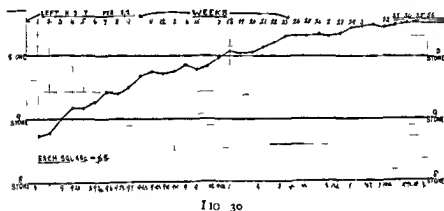


Chart showing increase of weight of patient after radium treatment of inoperable carcinoma *en cuirasse* of both breasts. The general condition improved rapidly and the patient is in good health and symptomless (Case of Mr Rock Carling)

weight chart (Fig. 30). The tumours in the breasts disappeared. There is some thickening of the skin and hardness of the breast. One year after treatment the patient is in excellent health.

Mrs C. H. age thirty-eight (Figs 27 and 28). Carcinoma of right breast adherent to skin and chest wall extensive dissemination along pectoralis major muscle and enlarged axillary glands.

Interstitial Dose — 7 560 mg hours. Complete disappearance of growth and glands (Recent case five months).

Miss R. E. age forty-two years. Carcinoma of left breast the size of an orange adherent to skin large mass of enlarged axillary glands. One gland excised for histological examination and showed secondary deposits of spheroidal celled carcinoma.

Interstitial Irradiation — Total dose 9 000 mg hours. Extensive peeling. Breast amputated three months later and showed no evidence of malignancy macro or microscopically.

TREATMENT OF POST-OPERATIVE RECURRENCES

The common types of recurrence are :

- (1) Cutaneous nodules in the vicinity of the operation scar
- (2) Supraclavicular glands
- (3) Ulcerating neoplasms near the sternum, involving cartilage or bone.

Dissemination with metastasis in the peritoneum, bones or chest are not considered, as these up till now are not suitable for radium treatment

TREATMENT**Cutaneous Nodules**

If the nodules are few in number, each one is irradiated by two needles of 13 mg of radium introduced into the tissues on each side and adjacent to the nodule. The needles are left in position nine days. This is followed by surface application by means of a Columbia paste cast placed over the area involved. If the nodules are very numerous surface application alone is used. Peeling is aimed at, the dose varying with the extent of the area treated.

Supraclavicular Glands

Surface application is employed. A Columbia paste collar is made covering the side of the neck and extending below the clavicle. Fifty mg of radium are necessary, sixteen to eighteen hours daily are given for twenty-one days. Average total dose, 12,000 mg. hours

Ulcerating Local Recurrence

In this type of recurrence much bigger doses are required. The treatment is by surface irradiation. As much as 40,000 mg. hours have been given. Recurrences which have been unsuccessfully treated with X-rays are still sensitive to gamma rays.

ILLUSTRATIVE CASES

Mrs R, age sixty-two years. Operated in 1916 for carcinoma of the right breast—radical amputation. Recurrence over sternum in 1924. Deep X-ray therapy failed to arrest progress of the disease

The condition before radium treatment was given was as follows Persistent pain over the chest and right arm large fungating ulcer 3 in by 2 in below the clavicle and to the left of the manubrium sterni The neoplasm was adherent to the chest wall and there was considerable hæmorrhage A total dose of 42 000 mg hours was given in twenty one days by means of Columbia paste The lesion healed in spite of chondro costal necrosis after removal of sequestra The patient is well and free from pain two years after treatment

Mrs B age seventy-one years Radical amputation of right breast in 1916 In 1922 recurrence in supraclavicular glands removed surgically In 1924 recurrence below the clavicle and in the posterior triangle of the neck The condition before radium treatment was as follows A mass the size of a pigeon's egg was present below the clavicle, near the acromion there was also a mass of hard glands in the posterior triangle of the neck marked pain in the arm and hand from pressure on the brachial plexus A total dose of 20 000 mg hours in twenty one days was given by surface application on Columbia paste This was followed by extensive peeling which healed in six weeks The masses below and above the clavicle entirely disappeared The patient is in good health two years after treatment

REFERENCES

- 52 DE NABIAS and HILFAGEL Le trait du cancer du sein par le rad
Le Cancer No 1 1925 p 3 and Trait par le rad de q neoplasm
Chahine Paris 1928 pp 75-89
- 53 KEYES G Rad Treat of Primary Carcinoma of the Breast
The Lancet July 21st 1928 p 108 and Rad Treat of Carcin
of the Breast *Rep Internat Conf Cancer* Lond 1928 pp 143-
145
- 54 WARD ROY Personal Communication
- 55 LEE BURTON Y Conservatism in the Treat of Primary Cancer of
the Breast *Rep Internat Conferen Cancer* Lond 1928 pp 131-
138

CHAPTER VIII

RECTUM

THE rectum is the commonest site of carcinoma in the alimentary canal, with the exception of the stomach. In nearly all the cases the growth is a columnar-celled carcinoma, frequently undergoing colloid degeneration. Carcinoma of the anus belongs to the group of squamous-celled carcinoma and is in a class by itself, especially in reference to treatment by radium. Carcinomata of the rectum are difficult to treat with radium owing to the radio-resistance of columnar cells. The radiosensitivity of the columnar-celled neoplasm is only very slightly higher than that of the normal mucosa of the rectum. This is responsible for the bad results obtained by many workers. Schwartz and Richard ⁵⁶ maintain, after a careful study of this subject, that surgical treatment ought to be given preference whenever possible.

The position of surgery in the treatment of cancer of the rectum is summarised as follows in the report on this subject published by the Ministry of Health ⁵⁷ in 1927.

The report is based on the examination of just under 6,000 cases of cancer of the rectum, in which operations for radical cure were performed in ten different countries. The findings of the inquiry are briefly as follows.

(a) On the average a period of twelve months was allowed to elapse between the occurrence of the first symptom of the disease and the patient coming to operation.

(b) Rather less than half of the cases when seen by surgeons were considered to be operable.

(c) About a sixth of all the patients who underwent a radical operation died as the result of such operation, or from causes connected with it. There is no doubt, however,

that it should be possible to secure a considerably lower operative mortality at the present time

(d) There is evidence, though limited, to show that the mortality from operation was much higher than the average among those patients who were in an advanced stage of the disease

(e) Two out of every five of those submitted to radical operation were alive three years afterwards

In the past the progress of radium therapy in rectal cancer has been hampered by serious complications. The complications were a painful post-irradiation proctitis, lasting several months, and occasionally radionecrosis of the coecum and sacrum. Early methods of treatment consisted in the introduction into the lumen of the rectum of a sound carrying radium tubes. This method, though in sporadic instances resulting in a cure, usually gives only palliative results and in the early days of radium therapy was frequently followed by radionecrosis due to insufficient screenage.

Proust⁵⁹ and de Nabris, by increasing very considerably the screenage and so using hard gamma rays, improved results, but obtained cures only exceptionally as the interstitial extension of the growth was never sufficiently irradiated. Laborde⁵⁹ increased the screenage to 2 mm. of platinum, and Quick used special rectal applicators so as to protect the normal mucosa. It was Neuman and Coryn⁶⁰ who first devised interstitial irradiation of the rectum from outside, and described a surgical approach facilitating needling of the rectal wall and the lymphatic areas. They met with considerable success, and in twelve cases where the rectum was removed after irradiation, no malignant cells could be found histologically.

Neuman and Coryn have treated up till now fifty-nine cases, their experience extends over five years, and their statistics are of unique value, as all the cases have been followed up. Of these fifty-nine cases, forty-six were inoperable or borderline cases. These authors obtained 20 per cent. cures after a three years' period. Their con-

clusions are : (1) That the results obtained by their method of treatment (colotomy, surgical approach, needling and subsequent excision) offer no advantage over surgical treatment. (2) In inoperable, extensive and fixed cancers irradiation combined with surgery of access is of considerable value.

Their technique was adopted with modifications of dosage by other workers. Sir Charles Gordon-Watson ⁶¹ has treated twenty-seven cases. Out of the first fifteen cases, including thirteen hopelessly inoperable, he records two cures of three and a half years' duration. He has made, however, a very important advance in the treatment of rectal cancer by demonstrating the possibility of avoiding colostomy. His views are crystallised in the following sentence. "Radical surgery for cancer of the rectum may be criticized on the score of mutilation in that a colostomy is essential and a reproach to surgery. Although I do not regard a well-managed colostomy as a great handicap in life, and I can produce many professional and business men, who follow their vocations with very little hindrance, to support this view, I do feel that when we see what can be done with the tongue, for example, we ought to explore the field of radium to the utmost in an endeavour to supplant radical surgery." ⁶¹ The difficulties in radium therapy of the rectum are much greater than those of other situations, such as uterus, mouth, larynx, owing to the difficulties of access. The results of treatment, though not to be compared with the above situations, are far less unsatisfactory than they were, owing to improvements in technique. Considerable progress has been made by submitting early and operable cases to irradiation.

The considerations guiding the choice of treatment at present are—(1) the good results obtained by surgical treatment alone in early cases; (2) the possibility of avoiding colostomy in early cases if radium treatment is substituted for excision; (3) the benefit of irradiation in borderline cases prior to operation; (4) palliation offered by radium in inoperable cases.

In the present stage of radium therapy operable cases should be submitted to irradiation (1) if operation is contra-indicated on general grounds, (2) if the patient is made to understand that results are uncertain, and operation may be necessary after irradiation, (3) to avoid colostomy in selected cases

If the growth is inoperable, radium is indicated in every case, as palliative results are obtained in the majority of cases

Colostomy

Up till recently a preliminary colostomy was a universally accepted necessity in all cases. It presents many advantages, by itself it is an excellent method of resting the rectum, eliminating the irritation of the growth by the faeces and preventing obstruction. In the majority of cases colostomy remains the first step of all treatment. Recently the writer, inspired by the results of Sir Charles Gordon-Watson, has treated three cases of carcinoma of the rectum with radium without preliminary colostomy. In this group the growths were limited in extent, of the cauliflower variety, and situated on the anterior wall of the female rectum. The possibility of avoiding a colostomy has therefore been demonstrated, but its elimination up till now is only possible in a few selected cases. Clinically carcinoma of the rectum and anus may be classified into three groups for the purpose of deciding what technique to adopt

- (1) Growths of the rectal ampulla
- (2) Growths of the anal canal
- (3) Supra-ampullary growth

TREATMENT

Ampullary Growth

Neuman's technique⁶⁰ remains up till now the best method of irradiation for this type of growth

FIRST STAGE COLOSTOMY

Median infra-umbilical laparotomy is performed the liver is examined for secondary deposits, the mesorectum

is carefully palpated and seeds or needles are introduced along the attachment of the mesentery (Sir Charles Gordon-Watson). If seeds are used they are left in position permanently ; if needles are used the linen threads are brought out through the lower end of the wound. The first stage of colostomy is then performed, the loop of sigmoid being brought out through a separate incision in the left iliac fossa. The median wound is closed.

[SECOND STAGE. SURGERY OF ACCESS AND IRRADIATION

Method of Neuman and Coryn.⁶⁰—This is carried out seven days after the colostomy. The operation is done

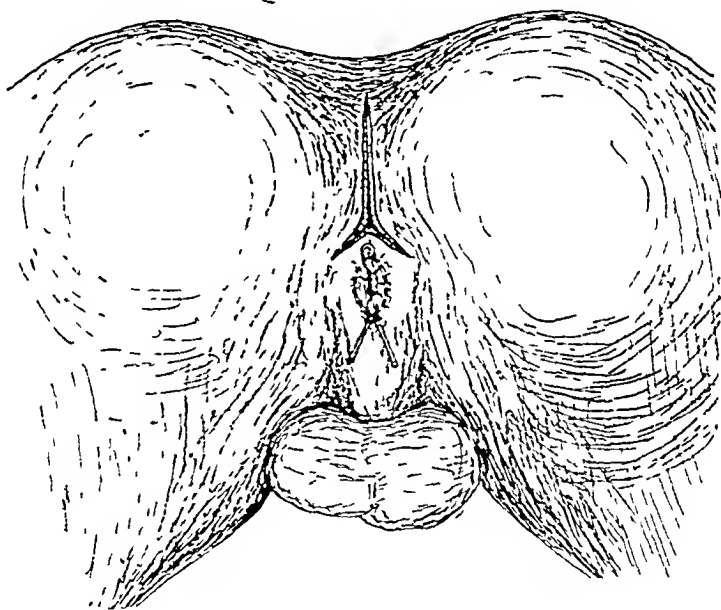


FIG. 31.—NEUMAN AND CORYN'S OPERATION
Incision. The anus is sutured. The patient is in the prone position.

under spinal anæsthesia. The patient is in the prone position, the buttocks at the end of the table and the legs widely separated.

Exposure of Rectum.—The anus is closed with a purse-string suture. An incision $3\frac{1}{2}$ in long is made over the coccyx vertically downwards to $1\frac{1}{2}$ in from the anus, here the incision bifurcates and extends down on either side (Fig. 31). The incision is carried through the skin and

subcutaneous tissues and exposes the coccyx, the median anococcygeal raphe, the insertion of the glutei maximi and levatores ani. The coccyx is resected and the finger separates the levatores ani, the median raphe is incised with scissors down to the external sphincter (Fig 32). The ampullary part of the rectum is exposed, by means of gauze swabs

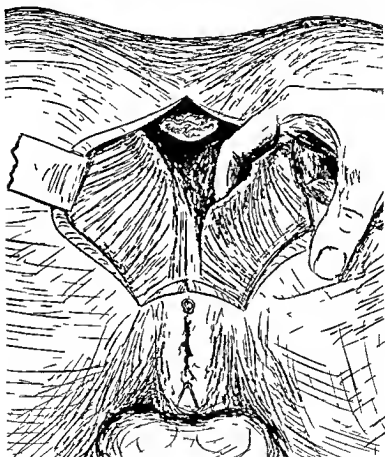


FIG 32 —NEUMAN AND CORY'S OPERATION

The coccyx has been removed. The median raphe is being incised

the rectal ampulla is mobilised and freed from its lateral and anterior attachments. In inoperable cases with anterior involvement of adjacent structures the skin incision encircles the anus, and this, together with the ampulla, is freed. By palpation the growth is carefully examined and its extent and volume ascertained.

Needling —(1) The growth itself is irradiated by means of

needles 16 mm. long containing 0.6 mg of radium and having a screenage of 0.5 mm. of platinum. These needles are introduced into the tumour, perpendicularly to the axis of

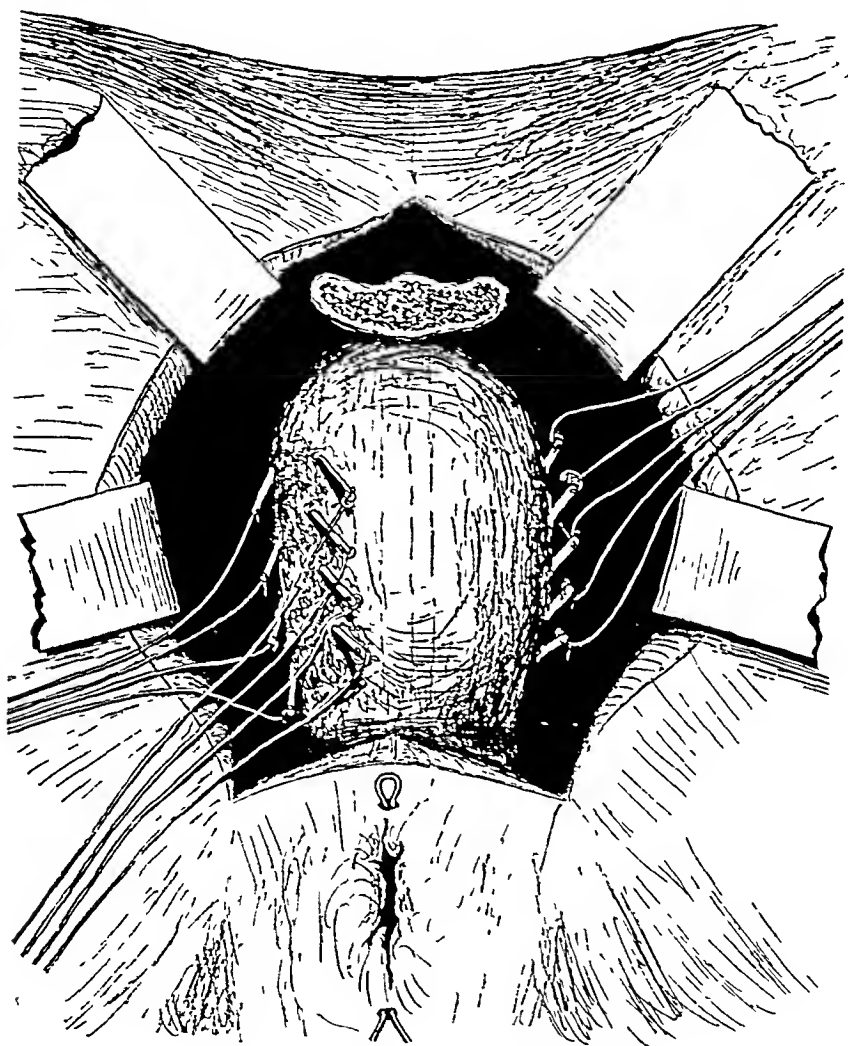


FIG. 33.—NEUMAN AND CORYN'S OPERATION

The rectum is free. The needles are introduced above and below and around the growth. The needles are shown half introduced, but should be completely buried in the wall of the bowel.

the rectum, if the volume of the growth permits it, otherwise the needles are introduced obliquely, they are placed at a distance of 1 cm. from each other and aim at a complete and homogeneous irradiation (Fig. 33)

(2) The rectum beyond the growth is irradiated by means

of needles 27 mm long containing 1.33 mg of radium, screened with 0.6 mm of platinum. These needles are introduced into the rectal wall, parallel to the long axis of the rectum, they are placed above, below and to the sides of the growth into apparently healthy tissue and into the peri-rectal cellular tissue (Fig 34)

(3) **Lymphatic Barrage**—Needles containing 2 mg of radium, 33 mm long, screened by 0.65 mm of platinum,

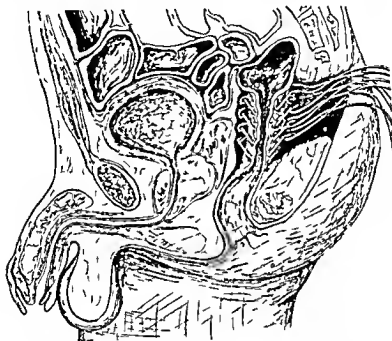


FIG 34—NEUMAN AND CORRY'S OPERATION. SIDE VIEW
The rectum has been freed all round. The needles are shown half introduced but should be entirely buried in the wall of the bowel.

are used. They are introduced (a) along the posterior wall of the rectum into the post-rectal space (concavity of the sacrum) on each side of the middle line, they are introduced upwards at a depth of 5 to 6 cm, they aim at the sterilisation of the meso-rectal lymphatics situated at the bifurcation of the superior hæmorrhoidal vessels (Fig 35), (b) into the upper part of the right and left ischio-rectal fossæ to irradiate the middle hæmorrhoidal area (c) in the lower part of the ischio-rectal fossæ—to irradiate the inferior hæmorrhoidal area.

All needles are threaded with linen threads soaked in flavine

Great care must be taken in inserting the needles to avoid entering the lumen of the bowel, and so prevent infection, which is an extremely serious complication. The rectum and threads are covered with a layer of sterile vaseline. The wound is packed lightly with gauze soaked in flavine and paraffin and partially sutured; one or two Carrel-Dakin tubes are left in between the layers of gauze. The outer layers of the dressing are changed daily, the remainder are left undisturbed except for the injection of Eusol solution through the tubes. The needles are not sutured in position, and the threads collected into two groups are brought out on each side of the wound

The patient is nursed on the right and left side alternately, but not on the back.

Dosage.—The average number of needles required for a complete barrage is .

15 needles at	0.6 mg.
15 needles at	1.33 mg
12 needles at	. 2 mg.

containing a total of 52 mg of radium. The needles are left in position seven days. The average total dose given is 10,000 mg hours

After Treatment.—The needles are removed on the seventh day and the wound irrigated daily with a mild antiseptic through the rubber tubes. When clean the tubes are removed and the wound allowed to close.

Vaginal Route

In suitable cases of anterior carcinoma of the rectum it is possible and advantageous to irradiate the tumour through the vagina. This is preferable to the separation of the rectum from the vagina for reasons of simplicity of technique. The needles are introduced through the vagina, a finger in the rectum controlling and guiding the distribution of radium (Fig 35)

Anal Growth

This type is a squamous-celled carcinoma, and responds more readily to irradiation. Treatment is carried out in two stages —

1st Stage—Colostomy can be avoided in suitable cases. The anal canal and growth are surrounded by needles containing 133 mg of radium element. They are inserted into and around the growth and into the ischio-



FIG 35

Two needles are shown in position behind the rectum in the concavity of the sacrum. The posterior part of the rectum is irradiated after removal of the coccyx. The anterior part and growth are irradiated from the vagina.

rectal fossa. The threads are attached to the healthy skin by means of collodion. They are left in position five days, and the patient is kept constipated with opiates. The average total dose is 3,500 mg hours.

2nd Stage Surface Application—After removal of the needles, surface irradiation is carried out without delay. A plaque of Columbin paste 15 mm thick is made, covering the sacrum and perineum, two other plaques are made for the right and left inguinal regions. The posterior plaque

carries 40 mg. of radium in numerous small needles, each inguinal plaque has 30 mg of radium. Irradiation by all three plaques simultaneously is given for a period of ten to fourteen days, the patient receiving eighteen hours daily. Average total dose. Posteriorly, 9,000 mg. hours, anteriorly, 6,900 mg. hours on each side. If the inguinal glands are enlarged and presumed to be infected with secondary deposits, the inguinal dosage is increased to 12,000 mg. hours on each side.

Supra-ampullary Growth

For growths situated high up in the rectum, and pelvic-rectal growths which extend above the peritoneal reflection, intra-abdominal irradiation presents the advantage of simplicity and permits a more extensive and regular distribution of radium needles.

The method as described by Sir Charles Gordon Watson ⁶¹ is as follows. "After laparotomy in the Trendelenburg position and an examination of the liver, the intestines are packed off and the meso-rectum and meso-sigmoid examined for glandular metastasis. Wherever required, needles are passed into the mesentery in apposition with the glands, the growth is then attacked systematically and a uniform barrier secured. The pelvic colon is then fixed ready for colostomy, but not opened. The needles have threads and beads attached which are brought out through the abdominal wall and sutured beneath the skin. The radium is removed after from seven to fourteen days, according to the amount employed without reopening the abdomen. The colostomy is left unopened as long as possible." In some cases it is not necessary to open the colostomy and the bowel is allowed to recede back into the peritoneal cavity (Fig. 36).

Combined Methods of Treatment

The oldest method of treatment, by intrarectal application of radium in larger doses efficiently screened although ineffective *per se*, has still a very useful place in the treatment

of cancer of the rectum. Alone it has given occasionally remarkable results, and it is a useful palliative measure in hopeless cases, it produces retrogression of the growth,

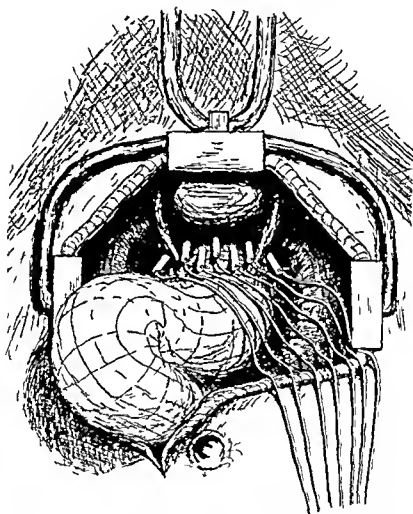


FIG 36—INTRAPERITONEAL NEEDLING OF SUPRA ANULLARY CARCINOMA OF THE RECTUM

Method of Sir Charles Gordon Watson. The needles are shown half introduced. They should be completely buried in the growth, care should be taken not to penetrate the lumen of the bowel. Needles are also inserted in the mesosigmoid and mesorectum.

diminishes hæmorrhage, discharge and pain, and in rare instances transforms an inoperable case into one suitable for surgery of access. It should never be used concurrently with needling, but may be employed before or after a needle barrage.

Treatment of Recurrences

Radium treatment may be considered as a useful method of treatment of cases which have recurred after operative treatment. The treatment is only applicable to local recurrences in the area of the operation. The method employed is a combination of needling of the scar, surrounding tissue and ischio-rectal fossæ with a surface application by means of Columbia paste to the perineum and inguinal regions. Retrogression of the growth is obtained. Dosage should be moderate and should not exceed 15,000 mg hours, given in seventeen to eighteen days, as, owing to presence of scar tissue and diminished blood supply, a radium burn is easily produced.

ILLUSTRATIVE CASES

Mrs A M B, age fifty-four years. Under the care of Sir Charles Gordon-Weston. Carcinoma of the rectum extending from 2 in above anal margin upwards for 4 in, most of the growth is on the anterior wall of the rectum, below peritoneal reflection, no glandular involvement, no hepatic deposits. Colostomy followed three weeks later by irradiation by **vaginal route**. Ten needles containing 20 mg of radium inserted into and around the growth and left in position fourteen days. Total dose, 6,720 mg hours. Rectal examination three and a half months later reveals no growth. Weight increased by 2 st. Fifteen months after treatment slight stenosis of rectum, no ulceration. Sixteen months after treatment colostomy closed at patient's request. Death from internal hæmorrhage five days after operation. The appearance of the rectum is shown in Fig 37. There is no evidence of any disease. Microscopical examination (Dr Cuthbert Dukes) does not show any evidence of a neoplasm. In the area treated the normal epithelium of the bowel has disappeared with the exception of a few islands of columnar epithelium, a thin layer of fibrous tissue forms the new lining of the bowel. The lymphatic glands in the extra-rectal tissue are in an atrophic condition and show no secondary deposits.

Mrs H E G, age thirty-nine years. Under the care of Sir Charles Gordon-Watson. Inoperable carcinoma of the rectum, extending from 2 in above the anal margin, upper limit of the growth not defined. Growth completely encircling the bowel and fixed. No hepatic deposits. After preliminary colostomy, radium barrage by **posterior route**; thirty needles containing 56 mg of radium left in position seven days, two needles at 5 mg each inserted through vaginal fornices and left in position three days. Total

dose 7104 mg. hours. Six months after irradiation rectal examination reveals stenosis of the rectum but no evidence of growth. General health good. Increase in weight of 2 st. Remains well till present day (two and a half years).

Mr B. B., age forty-four years. Under the care of Sir Charles Gordon Watson. Inoperable carcinoma of the rectum extending from 3 in. above anal margin to above peritoneal reflection, com-

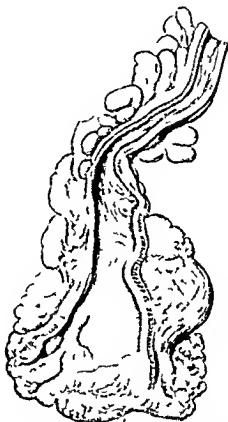


FIG. 37.—CASE UNDER THE CARE OF SIR CHARLES GORDON WATSON.

Appearance of rectum sixteen months after radium treatment for an ampullary carcinoma. There is no evidence of disease and no ulceration. Histologically no malignant cells found.

pletely encircling the bowel, firmly adherent to bladder and sacrum. Colostomy and intra-peritoneal insertion of radium by the abdominal route. Nine needles containing 20.5 mg. of radium left in position 115 hours. Total dose 2357 mg. hours. Six weeks after irradiation no growth detected on rectal examination. Patient remains well up till present day (eleven months). Sigmoidoscopy shows no evidence of disease.

Mr T. W., age sixty-four years. Eight years' history of rectal dis-

charge Carcinoma of the rectum 4 in from anal margin, entirely encircling the bowel, fixed anteriorly and posteriorly. Inoperable. Marked loss of weight. No evidence of secondary deposits.

Colostomy performed. Twelve needles of 2 mg. radium element each, screened by 0.5 mm. of platinum, 1 mm. of brass and 1 mm. of rubber introduced **into the lumen of bowel** and passed into the growth. Continuous irradiation for eleven days. Total dose, 6,336 mg. hours. Hæmorrhage ceased ten days after irradiation. Rectal examination four months after treatment reveals a fibrous constriction at the site of the growth which has completely disappeared. Well, eight months.

Miss S., age seventy. Carcinoma of the rectum. Ulcer, 3 in. by 2 in., on the posterior wall. Patient refused colostomy. Radium applied by **Neuman and Coryn's method**; 40 mg. of radium in needles of 0.6 mg., 1.3 mg. and 2 mg. inserted. Patient died on the sixth day of treatment from cardiac failure.

Post-mortem examination showed remarkable changes in the lesion, which, although it had only received 4,800 mg. hours, was a flat superficial ulcer, the redundant mass of growth having disappeared.

REFERENCES

- 56 SCHWARTZ and RICHARD. *La Vie Med.*, October 16th, 1925, p. 1656.
57. "Cancer of the Rectum." *Reports on Public Health and Medical Subj.*, H.M. Stat. Off., 1927.
- 58 PROUST, quoted by A. CHALIER and H. MONDOR. "Cancer du rectum," Doin, Paris, 1924, p. 456.
- 59 LABORDE, S. "La Curietherapie des Cancers," p. 253.
60. NEUMAN, F., and CORYN, G. "The Radio-surgical Treatment of Cancer of the Rectum." *Rep. Internat. Conferen. Cancer, Lond.*, 1928, pp. 128-130.
- 61 GORDON-WATSON, SIR CHARLES. "Radiation in the Treatment of Cancer of the Rectum." *Rep. Internat. Conferen. Cancer, Lond.*, 1928, pp. 100-106; and *Proc. Roy. Soc. Med.*, 1927, 21, pp. 9-16.

CHAPTER IX

PROSTATE, BLADDER, PENIS, URETHRA, VULVA, VAGINA

PROSTATE

THE treatment of carcinoma of the prostate is primarily surgical. Radium therapy has a place in the treatment as a palliative measure in inoperable cases, and gives definite beneficial results in the arrest of hæmorrhage and relief from pain. Histologically, carcinoma of the prostate is of the alveolar type not unlike that of the breast, and the response to irradiation is quite good. The paucity of the results obtained are due to the development of metastases in bones, to infiltration of the pelvic fasciæ and periprostatic tissues. Inoperability and extraprostatic extension are no contra-indication to radium treatment, on the contrary, they place the case into the group where radium is the first line of attack. There is also the group of cases where surgical removal of the prostate must not be undertaken owing to renal inefficiency, these cases may be submitted to radium therapy without undue risk.

The methods of irradiation vary with individual technique. Intra-rectal and intra-urethral application is most unsatisfactory, it attacks the normal mucous membrane of the rectum and urethra more readily than it produces an arrest of the growth of the neoplasm. They have been abandoned by most workers. Massive irradiation by the introduction of large quantities of radium (25 and 50 mg) is to be condemned here as nearly everywhere else, and for the same reasons. Multiplicity of foci, adequate screenage, careful distribution of needles, prolonged period of irradiation—these are the principles of irradiation of the prostate if the optimum effects are to be obtained.

Technique

Closed Method.—Marion ⁶² advocates the introduction of a tube of radium into each lobe of the prostate by means of a trocar and canula, through the perineum. De Nabias ⁶³ has developed this method, and introduces four tubes of 10 mg. each by means of a trocar by the perineal route. The dose recommended is 12,000 mg. hours in twenty-one days. A catheter is tied in the urethra for five weeks, being taken out two weeks after the removal of radium. He places great importance in the avoidance both of an incision in the perineum and also of suprapubic cystostomy.

Open Method

Transvesical Method.—Laborde ⁶⁴ advises the suprapubic approach, quoting two favourable results. This method has very little to recommend it unless the prostatic growth has actually invaded the vesical mucosa. It is followed by severe cystitis and prolonged convalescence.

Perineal Route.—Papin ⁶⁵ described, in 1922, a method of introducing radium tubes or needles into the prostate by open perineal operation. Maurer ⁶⁶ advocates the perineal method by open operation. He introduces in each lobe two tubes of 5 mg. each screened by 2 mm. of platinum. The tubes are left in position fifteen days, and the total dose given is 7,200 mg. hours. This technique was modified and improved by Gaudy and Van Dooren.⁶⁷ It necessitates a preliminary suprapubic cystostomy; this has many advantages; amongst them the relief of pain from spasm of the vesical sphincter during irradiation. A transverse incision is made in the perineum, the urethra is identified, and by means of an intra-urethral sound is pulled forward and upward; by blunt dissection the rectum is separated from its anterior connections and the prostate exposed. A flat retractor is introduced into the space between the rectum and prostate and needling is proceeded with. Six to ten needles each containing 1.33 mg. of radium are introduced into the prostate, and care is taken not to perforate the base of the bladder. The needles are not sutured,

but the threads are left sufficiently long to be strapped to the inner side of the thigh. The wound is lightly plugged and partially sewn up (Fig. 38).

The needles are left in position eighteen to twenty-one days. The average total dose given is 7,000 mg. hours. The suprapubic cystostomy is not allowed to close for at least two months after cessation of treatment.

Results—The immediate results are good. By rectal

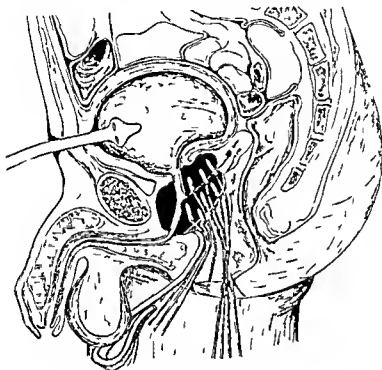


FIG. 38.—IRRADIATION OF PROSTATE BY THE OPEN PERINEAL METHOD. A De Pezzer's catheter is inserted suprapubically. The prostate is exposed from the perineum. Radium needles are shown in position.

examination it is possible to follow the changes in the size, shape and consistency of the prostate. Changes are first noticed in the third week of treatment. At the end of one month the prostate appears smooth and softer and has appreciably diminished in size. Hematuria is diminished or has stopped altogether. Cystitis is an inevitable consequence of the cystostomy, but it is not alarming. Perforation of the rectum or bladder from radio-necrosis does not occur if the needles have at least 0.6 mm. of pla-

tinum screenage Vesical fistula from perforation by the needles is avoided by careful technique. Spasm of the vesical sphincter is very difficult to avoid entirely, but can be remedied by the administration of belladonna or the local installation of cocaine. Normal micturition is established in about three months. End-results are more difficult to estimate, partly owing to death from urinary sepsis and debility, partly to the appearance of metastases

On the whole, the results are not so good as those in the tongue, larynx and uterus. Life is prolonged in general by two to three years. Sporadic cases of cures are reported from time to time, thus Barringer⁶⁸ reports four cases of cures up to periods of five years; Sluys and Van Den Branden⁶⁹ reported two cases of cure up to two years, Desnos⁷⁰ reports twelve cases cured out of a total of forty-four patients treated. These results compare favourably with surgical removal; in a series of 1,000 cases analysed by Bumpus,⁷¹ operative treatment gave a post-operative length of life of thirty months, Romanis and Mitchiner⁷² state that "treatment is of little avail, and death ensues in about a year or eighteen months."

BLADDER

Carcinoma of the bladder is usually of the squamous-celled variety, the columnar-celled type (adeno-carcinoma) being only very rarely met with in growths arising in the tubular glands at the base of the bladder. Occasionally a spheroidal-celled growth is also seen. The commonest type is the most radiosensitive, the others markedly less so. Clinically the papillomatous type is of better prognosis than the nodular or infiltrating variety. Sepsis is invariably present and complicates treatment. Radium treatment is contra-indicated in the presence of bilateral infection of the kidneys or if the urinary function is so impaired that surgery of access is too grave a risk. In no other localisation has radium treatment been more maligned than in cancer of the bladder, it is difficult to find a modern

surgical text-book or report on bladder growths without a reference to the futility or danger of radium treatment. These statements may have been true in the past, like similar statements and warnings in the cases of lingual cancer. To-day, radium therapy of bladder cancer shows results as good if not better than surgery—but only in the hands of experts, doubly expert both in urological surgery and in radium therapy.

Barringer⁷³ in a recent communication reports 75 per cent of cures, the majority over five years, in cases of papillary carcinoma and 35 per cent of cures (majority over five years) in infiltrating carcinoma, he considers radium as 'the method of election' in the treatment of bladder carcinoma. The difficulties in treatment are due to periodical distension, stretching and contraction of the bladder, and also to sepsis, which is an invariable accompaniment of malignant disease in this situation.

Methods of Treatment

Endoscopy

The introduction of radon seeds through an operating cystoscope has naturally attracted a great deal of attention from the urological surgeon. The method has a very limited field of usefulness, in small growths situated in an accessible portion of the bladder, in cases with little or no cystitis and good bladder capacity. The use of bare tubes has been abandoned even in America owing to burns, fistula and other complications, even gold tubes are not sufficiently well screened for this situation. The platinum seed with full protection (1 mm. of platinum) is the only one to be recommended. The seeds are introduced into and around the growth by means of an operating cystoscope. Special instruments have been devised by many workers, of these the cystoscope of Joseph Muir is perhaps the best. Dosage varies with the size of the tumour. The seeds used are of 2 M.C. initial strength, they are placed 1 to 1.5 cm. apart.

Cystostomy

This is the method of choice in a large majority of cases ; it is the only method in cases of cancer in the neighbourhood of the internal meatus and in the presence of hæmorrhage, sepsis or for the treatment of a large growth. The bladder is opened by the suprapubic method ; wide exposure and a good light are essential. In the presence

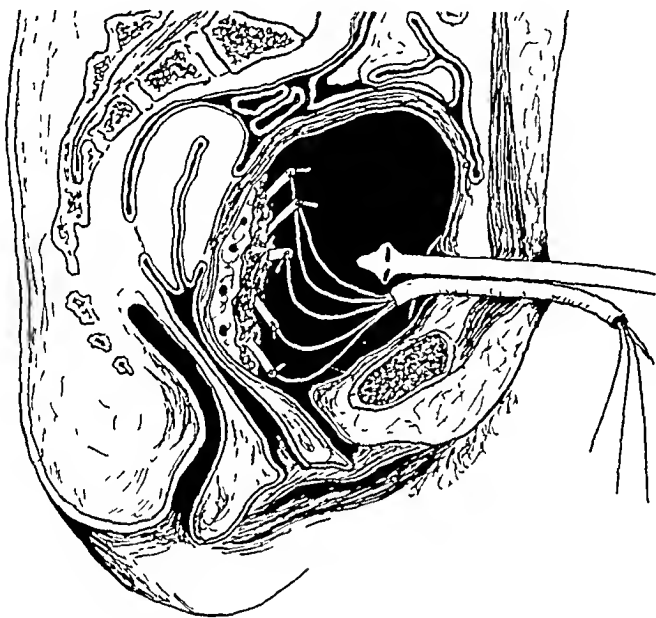


FIG 39 —OPEN SUPRAPUBIC METHOD OF IRRADIATION FOR CARCINOMA OF THE BLADDER

The needles are introduced into and around the growth. In the drawing the needles are shown half introduced, but should be entirely buried into the growth. Threads are brought out through separate rubber tube at the side of the De Pezzer.

of a papilliferous growth, the redundant part of the neoplasm is removed either by diathermy, cautery or the knife. Radon seeds or small needles containing 0.5 or 0.6 mg of radium are introduced into and around the growth. The threads attached to the needles are passed through a small soft rubber tube, and this, together with a De Pezzer's catheter, are brought out at the lower end of the wound, the rest of the bladder is closed (Fig. 39)

PLATE X

Epithelioma of Penis — Mr. Arthur Evans' case

A Before treatment

B Four months after treatment

PLATE X



growth. The Columbia paste plaques are applied sixteen to eighteen hours daily for eighteen to twenty-one days. The average total dose given to each inguinal area is 14,000 mg. hours. The suprapubic cystostomy is allowed to close at the end of a month. Urethral dilatation should only be done if there is serious risk of a stricture, and this is exceptional if the radium is well screened. Circumcision after irradiation is advisable, but should not be done till three to four months after the cessation of treatment.

FEMALE URETHRA

Carcinoma of the female urethra presents itself clinically as a polypus, an ulcer or a solid tumour. Venot and Parcellier ⁷⁵ recognise two types: (a) the vulvo-urethral, (b) the intra-urethral. Both are of the infiltrating variety and cause pain, dysuria, early hæmorrhage and occasionally retention of urine. Histologically, the growth is a squamous-celled carcinoma, occasionally there is an alveolar arrangement of the cells. The writer has seen one case of spheroidal-celled carcinoma secondary to a carcinoma of the breast amputated six years previously; this secondary deposit was a typical mammary cancer and responded well to radium treatment. The condition is rare, but seems to be more common recently. Up till 1925, 105 cases have been reported, since then the author has treated four cases and has seen three others. Pomeroy and Milward ⁷⁶ report a case of carcinoma of the urethra in an old negress treated successfully by radium. Fletcher Shaw ⁷⁷ reports two cases treated by radium. Eden ⁷⁸ in a discussion at the Royal Society of Medicine, states "this condition could be most hopefully treated by combining operation with irradiation, radium being used for the region of the primary growth." The writer ⁷⁹ has treated three cases with radium in the past four years.

Treatment

A suprapubic cystostomy is performed. The growth is surrounded with needles containing 0.6 mg. of radium,

PLATE XI

Primary Malignant Mass of Glands in Inguinal Region in a man
seventy-nine years of age Mr G T Mullally's case Con-
dition before treatment

PLATE VI



LUPIN

screened to 0.5 mm. and the needles are round the external meatus and the long axis the urethra. The needles are placed up to the bladder the needles are not to touch the vaginal wall. The needles are left in position which are collected out and the needles are left in position for 24 hours. The total dose is 1000 mg. for 24 hours. The dose is dispensed with at the end of 24 hours.

The treatment of lymphoma is the same as that described for secondary carcinoma of the penis. Both inguinal regions are treated with paste plaques. It is decided upon this should be done 4 weeks after irradiation. The removal of the glands at this time is inadvisable as the inter-lymphatic drainage affects adversely the growth of the primary growth.

VULVA

Epithelioma of the vulva of the squamous type. The majority of cases present itself as a cauliflower growth or an intertrigo. Surgical excision was considered the treatment of choice. Radium therapy proved what can be accomplished in inoperable cases. In combination with surgical excision radium therapy may be employed before or after operation. Delporte and Cahen⁸⁰ advise radium first and surgical excision after cicatrization of the lesion. Proust excises the inguinal glands and then irradiates the primary growth. De Nabias⁸¹ relies entirely on irradiation. Bailey and Bagg⁸² utilise radon seeds, and state that with seeds of 0.5 MC the primary growth can be made to disappear entirely.

A combination of diathermy excision followed by irradiation was practised by the writer in early cases but this method was abandoned in favour of irradiation alone.

Treatment

The primary growth is needled with 0.6 mg needles ; the periphery of the tumour is surrounded by needles containing 1.3 mg of radium. The number of needles varies with the extent of the lesion , treatment is continued for ten days The average total dose is 6,000 mg hours.

The inguinal glands are treated by surface irradiation with Columbia paste plaques, as described under the treatment of the inguinal regions in cases of epithelioma of the penis.

VAGINA

Epithelioma of the vagina is met with in a number of cases independently of carcinoma of the uterus. Radium treatment gives good results in cases of the cauliflower type , infiltrating growths require much larger doses, and to avoid urethral, rectal or vesical fistula adequate platinum screenage is essential

Treatment

A Columbia paste model is made to fit loosely the vaginal canal Twenty to 40 mg of radium are introduced into the model so as to lie opposite the growth. If the growth is on the anterior vaginal wall the posterior part of the model is covered with lead sheeting and *vice versa*. The apparatus is worn for seven to ten days ; it is removed daily to permit vaginal douching and is cleaned with lysol. Average total dose, 6,000 to 8,000 mg. hours

ILLUSTRATIVE CASES

Carcinoma of the Bladder

Mr C Y , age fifty-three years Seven months' history of hæmaturia and cystitis Cystoscopy showed an ulcerating nodular growth on the posterior wall of the bladder above the trigone and hiding right ureteric orifice Generalised cystitis Irradiation by open cystostomy

Nine needles at 0.6 mg of radium element introduced , bladder drained by De Pezzer's catheter Needles removed on the eighth day Total dose, 1,038 mg hours Suprapubic wound allowed to close at the end of the third week Hæmaturia ceased five days after introduction of radium Cystoscopy three months later showed a

68

62

1

—

E

1 1

2

4

E

PLATE XII

The same patient as Plate XI five weeks later, showing disappearance of growth and extensive peeling after a total dose of 20,000 mg hours in eighteen days. The skin healed in four weeks.

PLATE VII



12 a e p 110

4

1. The first part of the document is a list of names and titles, including "The Hon. Mr. Justice" and "The Hon. Mr. Justice".

10

100

1

1

small clean ulcer Micturition normal Cystitis greatly improved
(Recent case four months)

Epithelioma of Penis

Mr H W W age sixty one years Under the care of Mr Arthur Evans (Plate VII) Twelve months history of difficulty in micturition Ulcer noticed three months Epitheliomatous ulcer of glans penis surrounding and involving urinary meatus Enlarged glands in both groins femoral glands enlarged on right side Mass of glands palpable on the right side above Poupart's ligament (iliac glands)

Biopsy—Squamous celled carcinoma

Treatment—Suprapubic cystostomy Irradiation with ten needles of 0.6 mg. of radium element each left in position fourteen days Total dose to primary growth 2.016 mg. hours One gland from right inguinal region removed for histology and showed secondary deposit of squamous celled carcinoma

Surface irradiation of both inguinal regions by Columbia paste 4.000 mg. hours to each side (This in view of subsequent recurrence was an insufficient dose) The primary lesion healed entirely The condition before and after treatment is shown in Plate VII The patient remained well for twelve months He was then readmitted to hospital with suppression of urine bilateral decapsulation was done, but patient died of uræmia A post mortem examination showed an extensive bilateral pyelonephritis from constriction of the ureters by malignant disease in the pelvis Secondary deposits were also present intraperitoneally There was no recurrence of the penile lesion

Mr J C age fifty eight Under the care of Mr G T Mullally Seven weeks history of sore on penis and dysuria Epitheliomatous ulcer the size of a shilling near and around the meatus Suprapubic cystostomy and interstitial irradiation with seven needles of 0.6 mg. of radium element each left in position nine days Total dose 992 mg. hours

Small gland in the groin excised histologically inflammatory changes but no secondary deposit The penile lesion healed rapidly and entirely Well one year and eight months

Carcinoma of the Urethra

Mrs M M age fifty nine years Three months history of painful and frequent micturition discomfort when sitting down and occasional bleeding from urethra Small red ulcerated mass to the right of external meatus induration around meatus and extending along urethra for 1 in. No palpable inguinal glands

Biopsy—Squamous-celled carcinoma

Treatment—Suprapubic cystostomy Interstitial irradiation with six needles of 0.6 mg of radium element each introduced antero-posteriorly around external meatus. Needles left in position seven days De Pezzer's catheter removed three days later Total dose, 604 mg. hours. Complete disappearance of growth. Normal micturition. Well, twelve months

Mrs. R. S., age fifty years Spheroidal-celled carcinoma of the urethra following amputation of the breast for carcinoma four years previously. The secondary deposit involved the anterior two-thirds of the urethra and caused complete retention of urine There was also a small secondary deposit on the posterior vaginal wall

Biopsy.—Spheroidal-celled carcinoma

Intravaginal Surface Application—By means of a wax mould carrying 16.5 mg. of radium left in position nine days Total dose, 3,564 mg. hours The vaginal growth completely disappeared but the urethra was still hard although much smaller in bulk, and there was still retention of urine A suprapubic cystostomy was performed and the urethra and part of the vagina were excised Histological examination showed no malignant cells in the vagina but a well-marked deposit of spheroidal-celled carcinoma in the urethra The patient remains well two and a half years after treatment (that is, six and a half years after the original amputation of the breast).

This case illustrates that surface application with wax moulds, although an efficient method of treatment for vaginal epithelioma, is not a suitable method for the treatment of the urethra, which should be irradiated interstitially

Epithelioma of the Vulva

Mrs. E. P., age sixty-nine years Under the care of Mr E. Rock Carling. Four years' history of ulceration of the vulva Epithelioma involving left side of vulva, chiefly left labium majus Leucoplakia of labia minora Palpable glands in both groins

Interstitial irradiation with thirteen needles of 0.6 mg of radium element each left in position ten days. Total dose, 1,672 mg hours

Surface application of both groins Total dose, 2,400 mg hours to each side Lesion healed rapidly (recent case, four and half months)

Epithelioma of the Vagina

Patient under the care of Mr Aubrey Goodwin Age sixty-two, married twenty-nine years Children two, the younger twenty years old. Menopause ten years ago at the age of fifty-two. Ad-

mitted to Chelsea Hospital for Women on January 23rd 1928 complaining of

- (1) Something in the front passage for four years
- (2) Watery brownish discharge from the vagina for six months,
- (3) Hemorrhage from the vagina continuously for the last four months

On examination General condition fair no obvious wasting, nothing abnormal in chest or abdomen, one enlarged inguinal gland on the left side

Vaginal examination showed a large sessile growth of the posterior vaginal wall extending from the posterior fornix to the vulval orifice. Oval in outline about 1.5 cm in thickness ulcerated and bleeding freely on examination. Cervix not involved body of uterus small and sessile. Transferred to Westminster Hospital at end of February. On March 2nd a piece of growth involving the whole thickness was removed for biopsy and 40 mg. of radium in fourteen needles were planted in a concave oval way plaque which was fitted accurately over the growth. The anterior vaginal wall was screened with a sheet of lead and the plaque left *in situ* for seven days. Four needles containing 5 mg. each and ten needles containing 2 mg. each were distributed around the *periphery* of the plaque and so arranged as to have a cross fire action. Total dose 6720 mg. hours. On removing the plaque at the end of the week the most marked change was a diminution of the thickness of the growth which had become almost flat. At the end of another week the enlarged inguinal gland was removed for biopsy and the vagina examined again under anaesthesia. There was a clean, smooth healing ulcer and by April the whole vagina was healed smooth and supple and showed no signs of growth. This condition still persists.

Pathological Reports—(1) Portion of growth Squamous carcinoma. (2) Inguinal gland Chronic inflammation

REFERENCES

62. MARION. D'un moyen simple et facile d'appliquer le Radium dans le Cancer de la Prostate. *T d'Urologie* Vol VII No 3 p 335
63. DE NABIAS S. Traitement par le Radium de quelques neoplasmes. Chahine Paris 1925 p 127
64. LABORDE S. La Curiotherapie des Cancers 1925 p 257
65. PALIN. Le Cancer de la Prostate et le radium. *Soc d'Urologie* December 11th 1922 and January 5th 1923. Quoted by Laborde
66. MAURER A. Cours de curiotherapie et de Radiotherapie penetrante. *Hopital Tenon* June 1923 Chahine Paris fasc 4 p 198
67. GAUDY J and VAN DOORSEN I. Traitement du Cancer de la Prostate. *Le Cancer* 1924 No 3 p 221
68. BARRINGER B. Carcinoma of the Prostate. *Surg Gynecol Obst* February, 1922 Vol XXXIV No 2 p 168
69. Reference in article by GAUDY and VAN DOORSEN in *Le Cancer* September 1924 p 232

- 70 DENOS "Traitement du Cancer de la Prostate par le Rad" *Twenty-first Con d'Urolog*, Strasburg, October, 1921 (quoted by Laborde)
71. BUMPUS, Jun, H C "Carcinoma of the Prostate" A Clinical Study of 1000 Cases *Collected Papers of Mayo Clinic*, Vol XVII., 1925, p 411
- 72 ROMANIS, W H C, and MITCHNER, P H *Sc and Pract of Surgery*, Vol II, p 873
- 73 BARRINGER, B S "End Results of Radium Removal of Carcinoma of Bladder" *J Am Med Assoc*, 1928, p 362
- 74 LE ROY DES BARRÈS and HEYMAN, P "Le Cancer de la verge au Tonkin" *J de Rad et de l'Electiog*, 1927, Vol XI, p 85
- 75 VENOT, A, and PARCELLIER, A "Le cancer de l'urethre chez la femme" *Rev de Chu*, 1921, 59, pp 565-623
- 76 POMEROY, L A, and MILWARD, F W "A Case of Primary Carcinoma of the Female Urethra treated with Radium" *Surg Gynec and Obstet*, 1922, 35, pp 355-357
- 77 SHAW, W F "Carcinoma of the Female Urethra with Notes of Two Cases treated with Radium" *J Obst and Gynecol Brit Emp*, 1923, 30, pp 215-219
- 78 EDEN, T W, in discussion *Proc Roy Soc Med, Sect Obst and Gynec*, 1925, Vol XVIII, No 8, p 47
- 79 CADE, S "Clinical Report on Cases of Carcinoma treated by Radium" *Reports of Brit Emp Can Camp*, 1927-28, p 62
- 80 DELPORTE, F, and CAHEN J "Le traitement radio-chirurgical des epitheliomes de la vulve" *Le Cancer*, 1925, No 2, p. 61
- 81 DE NABIAS, S "Traitement par le Radium de quelques neoplasmes" Chahine, Paris, 1928, p 98
- 82 BAILEY, H, and BAGG, H J "Vulval and Vaginal Cancer treated by Filtered and Unfiltered Radium Emanation" *American J Obst and Gynecol*, 1921, Vol II, No 6, pp 587-592

CHAPTER X

UTERUS

IN a prefatory note to the Report on Cancer of the Uterus by Dr J E Lane-Clayton,⁸³ published in 1927, Sir George Newman, Chief Medical Officer of Health, makes the following statement of great importance —

We shall see later that other important conclusions are drawn but confining ourselves for the moment to the results of radiological treatment in uterine cancer we find that broadly speaking the results obtained are the equal of those obtained by operation, viz survival to five years of about 40 per cent of patients suitable for operation. In addition survival to a similar period of about 12 per cent of patients who are inoperable is secured. Since recurrence of the disease after five years of freedom is comparatively rare it is reasonable to regard absence of the disease after an interval of five years from the event of treatment as having established a high probability of cure. Further radiological treatment supplies an efficient palliative in many cases in which cure cannot be hoped for. When it is remembered that effects of this order can be secured without many of the risks disadvantages and inconveniences attendant upon operative treatment, one is impelled to inquire whether these remedial agents radium and X-rays are used as widely as they should be and with similar results in England. It is clear that one of the most serious deterrents to patients needing early advice and treatment for cancer is the dislike of operation. If this fear can be removed by substituting another method of treatment a great impulse might be expected in the movement for securing the attendance of patients at hospital in an earlier stage of their malady.

Unfortunately it is difficult to ascertain the exact extent to which radiation is used in England still more difficult is it to obtain a knowledge of its results owing to the apparent and natural disinclination of surgeons and radiologists to publish accounts of series of cases. This in turn is no doubt due to the absence or incompleteness of clinical records and a system for ascertaining the after histories of treated patients. Such indications as are available seem to suggest that we are much less advanced in the treatment of cancer by radium than certain continental countries and probably keep less satisfactory records. If these impressions are confirmed by the acquisition of further evidence the position is one for some disquietude and for a serious and sustained effort to remedy the defects.

It is unnecessary to give any detailed account of the frequency of uterine cancer, its mortality, operative risks and percentage of cures. No one doubts the frequency of the disease, and the statistical data are available in numerous publications. The gravity of Wertheim's operation is not denied ; its efficiency to "cure" cancer of the cervix in a certain number of cases is well known. The possibilities of radium, on the other hand, are obvious only to those gynæcologists familiar with radium therapy ; the others are slow to acknowledge the possibilities of radium treatment in spite of international conferences and results published from numerous European and American clinics. Radium has been used for cancer of the uterus for over twenty years ; methods have varied with the gradual progress in technique. Large numbers of cases have been treated with satisfactory results, and the literature on this subject is very voluminous. Cures of five and eight years have been recorded as long as five years ago. It is a commonplace to state that the mortality of radium treatment is negligible and need not be compared with the mortality of Wertheim's operation. Wertheim's operation is possible in strictly operable cases ; radium therapy is applicable to inoperable and advanced cases. Radium therapy has rendered inoperable cases suitable for operation. More data are available for the treatment by radium of uterine cancer than for any other anatomical situation, and the efficiency of this method of treatment has been fully proved. The final decision, whether a given patient should be treated by radium, operation or by a combination of methods, rests with the individual gynæcologist. Those conversant with the possibilities of both radium and surgery are more likely to arrive at an unbiased conclusion.

CERVIX UTERI

Methods of Treatment

The methods of treatment vary with different clinics. The most important methods are —

(1) Intra-uterine and vaginal applications advocated by

Regaud ⁸⁴ and his associates, Proust and De Nabias ⁸⁵ and Laborde ⁸⁶

(2) Needling described by Delporte and Cahen,⁸⁷ of Brussels, and Malcolm Donaldson,^{88 89 90} of St Bartholomew's Hospital

(3) Intra-abdominal irradiation (Delporte and Cahen ⁸⁷)

Dosage

Irradiation for short periods of time by large quantities of radium is gradually being superseded by prolonged irradiation with small quantities of radium. Donaldson ⁹⁰ states that the 144 hours' treatment shows 19.6 per cent better results as compared to the twenty-four hours' treatment. The bomb method, in which 5 gr of radium element is applied daily for a short period of time, may in the end prove the most valuable form of treatment.

Technique

(1) Intra-uterine and Vaginal Application

In cases where the external os is not entirely hidden by the neoplasm, tubes containing 5 or 10 mg of radium, screened with 0.8 mm of platinum, are inserted into the cervical canal. As a rule not more than four tubes can be introduced. They are left in position four to six days. Total average dose, 5,000 mg hours (Fig. 40).

If the vaginal vault is involved in the growth and the cauliflower mass present entirely hides the external os, or the cervix is represented by a deep crateriform ulcer, surface application is employed. A wax model is prepared similar to that described for the treatment of epithelioma of the vagina. Forty mg of radium in numerous small needles are inserted into the wax model chiefly at the apex and the periphery. The apparatus is worn continuously for seven days, but is removed daily and a douche given. Total average dose, 7,000 mg hours (Fig. 40).

(2) Needling

The cervix and lower segment of the uterus are transfixed by needles containing 2 mg and 1.3 mg of radium,

screened by 0.65 mm of platinum. Ten to fifteen needles are necessary. A total of 35 mg of radium is left in position for seven days. Average total dose, 6,000 mg hours (Fig. 41)

(3) Intra-Abdominal Application

This method is supplementary to (1) and (2). A period of four to six weeks is allowed for cicatrisation of the

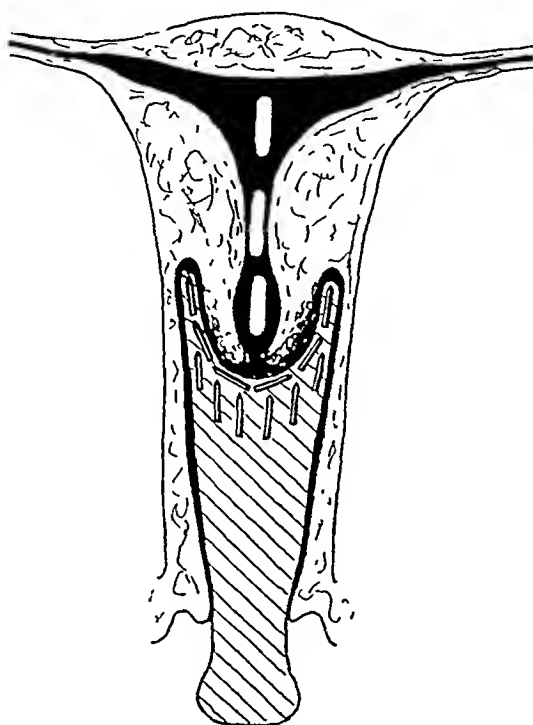


FIG 40

Diagram of uterus and vagina showing

- (1) Three tubes of radium in cervical canal and uterus, these are enclosed in a thin rubber tube, which for clarity sake has been omitted in the drawing
- (2) A wax mould containing radium. Needles are distributed at the periphery of the uterine end of the wax mould, and are placed at the requisite distance and aim at the irradiation of the growth and fornices

vaginal lesion. Laparotomy is performed in the Trendelenburg's position. The lower half of the uterus is needled with six to eight needles of 2 mg each, screened with 0.65 mm of platinum; the needles are placed anteriorly. The broad ligaments are incised, two or three tubes of

5 mg each or one or two tubes of 10 mg, screened with 1 mm of platinum, are placed on each side of the uterus, in between the two layers of the broad ligament (Fig 42). All needles and tubes have linen threads attached, these are enveloped in a sheet of thin rubber tissue. The abdomen is closed in the usual way, all threads and the end of the rubber tissue are brought out at the lower end of the wound. The radium is left in position for six to seven days. It is removed by traction on the threads after

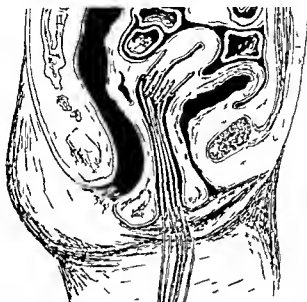


FIG 41—NEEDLING OF CARCINOMA OF CERVIX VAGINAL METHOD
The needles vary in length. Care must be taken not to perforate the bladder or rectum.

removal of the rubber tissue. Total average dose, 5 500 mg hours.

In addition, Stanley Dodd and Aubrey Goodwin⁹¹ recommend the removal of iliac and obturator glands if removable and ligation of internal iliac arteries. If not all the glands are removable, as many as possible should be dissected and the remainder surrounded with needles containing 2.5 mg of radium. Delporte and Cahen treat the vagina first, and this is followed by laparotomy. Dodd and Goodwin prefer to perform laparotomy first and to treat the vagina afterwards.

Results

(a) Immediate Effects

Hæmorrhage ceases in nearly all cases soon after the treatment. Donaldson states that in 85 per cent. of his cases bleeding ceased permanently or for a considerable

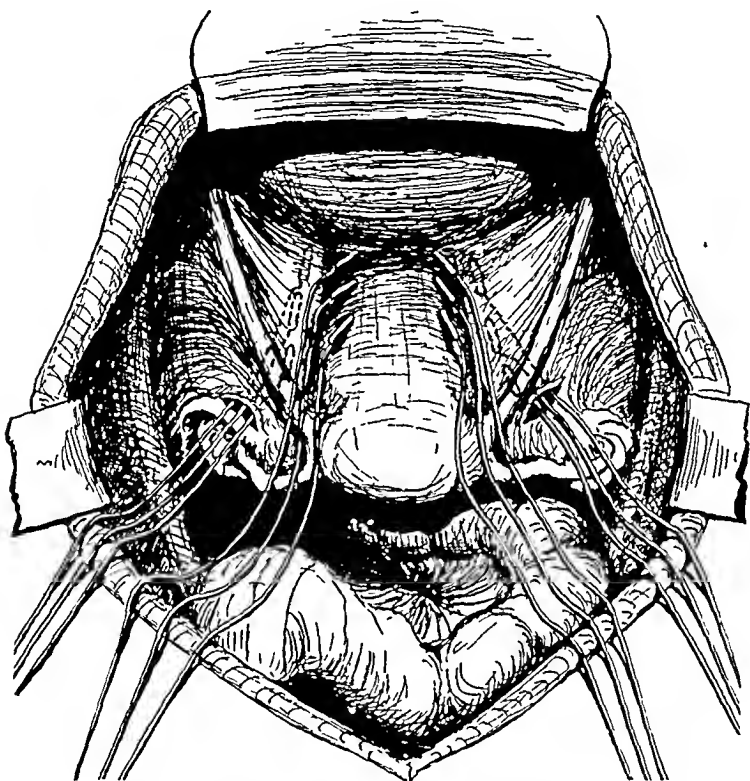


FIG 42—INTRA-ABDOMINAL IRRADIATION FOR CARCINOMA OF CERVIX UTERI

Needles are inserted into the lower portion of the uterus and into the cervix. The needles are shown half introduced, but should be buried entirely into the wall of the uterus. The broad ligaments are incised, and tubes inserted into the parametrium. These tubes can be enclosed in a rubber catheter, and the loaded catheter placed in between the two layers of the broad ligament.

period of time. Cauliflower growths disappear; ulceration heals. The general health of the patient improves.

(b) End Results

Heyman⁹² in 145 operable cases treated by irradiation alone obtained 46.2 per cent. of five years survival. Malcolm Donaldson⁹³ quotes 228 cases, 165 inoperable,

sixty-three operable, twenty-three operable cases treated by radium alone, five years' statistics are not given, but the results support those obtained by other observers

Regaud states a survival of three and a half years or more in 12 per cent of inoperable cases

Healy,⁸⁴ of New York, in an analysis of 224 cases, observed for five to six and a half years, arrives at the conclusion that irradiation offers better results than surgery

Combination of Methods

Pre-operative Irradiation transforms some inoperable cases into operable ones. It sterilises the growth, stops hæmorrhage, and by the improvement in general health diminishes the operative risk. Post-irradiation fibrosis is negligible if suitable dosage is given and if operation is not delayed for more than one month after irradiation.

Post-operative Irradiation is recommended by Dodd as a prophylactic measure to diminish the chances of recurrence. Recurrences treated by radium⁸³ give 15 per cent of recoveries at the end of three years and 55 per cent at the end of five years.

CANCER OF THE CORPUS

In this situation surgery gives better results than irradiation. The disease is less malignant and gives much better results with hysterectomy than the cervical variety. Radium treatment is only reserved for inoperable cases or as a pre-operative measure. In these forms short intensive irradiation presents advantages. Twenty-four hours treatment with 80 to 100 mg of radium as a preoperative measure does not in any way increase the operative difficulty and sterilises the endometrium.

REFERENCES

- 83 LANE CLAYTON J. E. Cancer of the Uterus. *Rep. on Public Health and Med. Subject No. 40* 1927 p. 1.
- 84 LACASSAGNE A. The Causes of Success or Failure in the Radiotherapy of Cancer of the Cervix Uteri. *Report Internat. Conf. Cancer* 1928 p. 82.

- 85 DI NABIAS, S "Traitement par le radium de quelques neoplasmes " Chahine, Paris, 1928, pp. 31-58
- 86 LABORDT, S "La Curiothérapie des Cancers," 1925, pp 231-242.
- 87 DELPORTE, F, and CAHUN, J "Traitement transabdominal des Cancers Inseparables du col uterin " *Le Cancer*, 1926, No 1, pp 21-54, and "Contrib à l'Etude epith cylindriques de l'uterus " *Le Cancer*, 1927, No 3, pp 306-327
- 88 DONALDSON, M "Treatment of Inoperable Cancer of the Cervix Uteri with Radium " *B M J*, May 9th, 1925
- 89 DONALDSON, M "The Treatment of Inoperable Cancer of the Female Pelvic Organs " *B M J*, November 7th, 1925
- 90 DONALDSON, M "The Radium Treatment of Carcinoma of the Cervix since 1921 " *St Bart's Hosp Report*, 1927, pp 97-112
91. DODD, S, and GOODWIN, A Personal communication
- 92 HYMAN "Acta Radiologica," Vol VIII, quoted by Malcolm Donaldson *Report of International Conf Cancer*, London, 1928, p 77
- 93 DONALDSON, M "The Advantages of Radiation in the Treatment of Cancer of the Cervix Uteri " *Report Internat Conf Cancer*, London, 1928, pp 75-81
- 94 HITALY, W. P "Classification and Radiation Treatment of Cancers of the Cervix Uteri " *Rep Internat Conf Cancer*, London, 1928, p 86
- 95 LANG-CLAYTON, J E "Cancer of the Uterus " *Reports on Public Health and Med Subject*, No 40, 1927, p 23

CHAPTER XI

ŒSOPHAGUS—STOMACH

ŒSOPHAGUS

As recently as 1926 Berard and Sargnon⁹⁶ from an extensive survey of published records of cases of cancer of the œsophagus concluded that there has not yet been a single case of actual cure by means of radium. The operative mortality of surgical removal of carcinoma of the œsophagus is, I believe, still 100 per cent. Theoretical operations described by some authors have no place in clinical surgery. Posterior mediastinotomy belongs to the latter group. Fodor Edwards has approached the thoracic œsophagus by the transpleural route which has the advantage of giving excellent exposure. But successful resection of part of the œsophagus by this route still remains a hope deferred. The classical treatment to day remains what it was fifteen years ago—gastrostomy or the introduction of some form of tube into the growth to permit swallowing. The question of early diagnosis cannot by itself be of great help in the therapeutics in this situation unless radium treatment is considered. Early diagnosis can be achieved with the help of radiology and œsophagoscopy but they can be so achieved only if the suspicion of œsophageal cancer is ever present in the clinician's mind, and no case of discomfort in deglutition is dismissed as "hysteria" till proved not to be organic.

Ledoux and Sluys⁹⁷ have described a radiological technique of "retrograde opaque meal" by which the lower limit of the growth can be localised, this is valuable if irradiation is to be complete and rational and is an essential preliminary to surgical approach of the œsophagus. Failures to cure œsophageal cancer by radium were inevitable as long as the irradiation consisted in the introduction

into the lumen of the œsophagus of a large quantity of radium Guisez,⁹⁸ who has used this method extensively (270 cases), had but very few successes till 1925. The failures of this method are due not to resistance of œsophageal carcinoma to radium, but to faulty irradiation. The extent of the growth cannot be estimated; uniform irradiation is not obtained, it is difficult to place the radium tubes in position, and still more difficult to keep them there for the required period of time. Radium burns result and fatalities are not infrequent. Renfern⁹⁹ reports two cases of radium necrosis of the heart following this method. De Nabias¹⁰⁰ describes a method of surface irradiation by Columbia paste applied on each side of the dorsal region of the vertebral column, this method has given no results. A great step in the progress of radium therapy in this situation was the introduction of radon seeds. Joseph Muir¹⁰¹ advocates the introduction of removable seeds through a special œsophagoscope of ingenious construction. He claims highly gratifying initial results. Herriman¹⁰² claims similar results. The advantage of this method is its simplicity. It fails inasmuch as it does not permit the distribution of the seeds in the depth of the œsophageal wall without undue risk of perforating the aorta or other neighbouring structures. Transpleural approach of the œsophagus as practised by Tudor Edwards is the best surgery of access available up till now.

Operation

The position of the growth is ascertained by radiography and œsophagoscopy. Preliminary to operation it is essential to extract all carious teeth and to get the mouth as clean as possible.

Side of the Operation.—Carcinomata, situated at the lower end of the œsophagus, are approached from the left side which gives an uninterrupted view of the œsophagus with very little traction of the pericardium. In this situation the aorta lies immediately behind the œsophagus. Tumours situated in the region of the bifurcation of the trachea are also approached from the left side. In this situation the tumour generally lies below the aortic arch, and by incising the pleura over the œsophagus close to the margin of the descending aorta a good view is obtained. For a growth situated above the bifurcation of the trachea but still within the chest the operation is

done on the right side. On this side the *Vena Azygos major* requires division between two ligatures before an adequate view is obtained.

Artificial Pneumothorax—The side of the operation having been decided upon the next step is the production of an artificial pneumothorax on the side chosen. The preliminary filling is done a week before operation and an average of 300 c.c. of air is introduced. a refill of 400 c.c. is given on the second, fourth and sixth days aiming at a pressure of about ± 1 mm. on the third refill. this produces a satisfactory collapse of the lung which should be controlled by X ray examination.

The best form of anaesthesia is intratracheal gas and oxygen combined with local injection.

Position of Patient for Operation—After induction of anaesthesia the patient is placed on the uncollapsed side with an air pillow under the axilla and the arm fully abducted. The arm on the collapsed side is allowed to drop across the body so as to rotate the scapula forwards as much as possible. The operator stands at the patient's back. The incision is made at the sixth intercostal space and extends from the nipple line to the outer border of the erector spinae. The cutaneous structures and latissimus dorsi are cut through. the 4th, 5th and 6th intercostal nerves are injected with 1 per cent novocaine. The chest is opened by an intercostal incision in the middle of the space and a rib spreader introduced. If this gives insufficient space one or two ribs above the incision are cut across but not removed. the intercostal vessels are ligatured. The growth is examined and its extent fixity and the involvement of surrounding structures ascertained. At this stage the anaesthetist passes an oesophageal bougie. The oesophagus or the vagi where visible are painted with a 0.5 per cent solution of cocaine. This is done to prevent impulses passing along the vagi. If the opposite pleura is inadvertently opened a positive pressure can be kept up through the intratracheal tube till the opening is sutured. Radon seeds are introduced into the tumour and above and below it. The seeds have an initial strength of 1.8 MC. and have a screenage of 0.5 mm. of platinum. They are left in position permanently. The number of seeds varies with the extent of the growth but ten or twelve are as a rule sufficient. The chest is closed. It is seldom practicable to suture the pleura but the approximation of the muscular layer is sufficient. this is done by continuous suture and before the last stitch is introduced the collapsed lung is blown out through the intratracheal catheter.

The operation produces severe shock.

STOMACH

One of the commonest forms of malignant disease is cancer of the stomach. In men it accounts for more than

one-third and in women for one-fifth of all cases of carcinoma. If left untreated it proves fatal within twelve months. Radiography is of the utmost importance in diagnosis; early diagnosis is exceptional, as the onset of the disease is very insidious. Surgical treatment has everything to recommend it; operative mortality is of secondary importance if the natural course of the disease is considered. End results of partial gastrectomy must be correlated with the extent of the disease at the time of operation, otherwise an apparent discrepancy is seen in the figures quoted by various writers. Fifteen per cent. of cures may be taken as a good average. Waring¹⁰³ considers this percentage too high. Balfour,¹⁰⁴ on the other hand, shows in a series of 1,000 cases a 52 per cent survival at the end of three years if the glands are not involved, and 19 per cent in those with secondary deposit in the glands. But partial gastrectomy is only practicable in a small number of cases. Excluding patients with hepatic secondary deposits, supraclavicular glands and ascites, there is left a group of cases where local extension of the disease or its high situation preclude surgical removal of the growth. In these cases a short-circuiting operation or jejunostomy is the only aid surgery can offer. It is a palliative measure of great benefit, it increases comfort and prolongs life for a brief period. Finally there are cases which recur locally after partial gastrectomy, and the "leather bottle" variety, which only very brave surgeons can hope to remove. An attempt to bring radium into the service of those afflicted with cancer of stomach is of necessity doomed to many disappointments—but no advance will be made if, after a single failure, radium is discarded. Radium therapy here, as elsewhere, demands years of efforts before a suitable technique is developed. The treatment by radium outlined here is no substitute for gastrectomy or gastrojejunostomy, neither is it a purely theoretical form of treatment. It is the first rung on the ladder of progress. Where it may lead eventually is a matter for speculation.

It has achieved something quite definitely beneficial as a form of palliation. Very few cases have been treated up till the present either in America, on the Continent or in this country. It is useless, therefore, to demand statistics, compare figures, calculate the percentage of survival. No figures are available, and the literature on the subject is meagre in the extreme. Radium treatment of cancer of the stomach is pioneering in an unknown territory, and the reward may be as great as that in cases of cancer of the uterus and tongue.

Selection of Cases

The cases submitted to irradiation fall into one of the following groups —

- (1) Carcinoma of the cardiac end of the stomach
- (2) Carcinoma of the pylorus not suitable for excision from local extension or adherence to surrounding structures
- (3) "Leather bottle" stomach
- (4) Local recurrence after operation

Treatment

In the treatment of cancer of the stomach by irradiation, radon seeds are of greater value than needles or tubes, and they are to be chosen if available. Needles present two disadvantages. (1) The necessity of their removal, which means either drainage or reopening the abdomen. (2) The necessity of protecting the surrounding area, this is difficult to realise in practice, but is essential because of the proximity of the liver and spleen to the source of irradiation, especially as prolonged irradiation is required, and the amount of gamma rays given off is maintained at the same level during the whole period of treatment.

Technique

Laparotomy is performed. It is advantageous to make a transverse incision cutting across both recti—it gives a very good exposure and subsequent healing is excellent.

The growth is examined, its extent and connections ascertained ; the liver is examined for the presence of secondary deposits. If the growth occupies the pyloric half of the stomach and localisation permits, gastrojejunostomy is performed, otherwise jejunostomy is resorted to, but if this is necessary it is the last stage of the operation. Radon seeds are introduced into the growth, around it and along the lesser and greater curvatures ; the gastro-hepatic omentum is examined and seeds introduced near its attachments (Fig 43). The number of seeds varies with the extent of the growth ; the seeds are screened with 0.5 mm.



FIG 43

Skiagram showing twenty platinum seeds in a pyloric carcinoma and along both curvatures. The seeds are left in permanently.

of platinum, have no terminal threads and are left in permanently. The seeds are of 1.2 M.C. initial strength. The abdomen is closed without drainage.

An alternative method, suitable for movable pyloric growths only, is to bring the pyloric portion of the stomach outside the parietal peritoneum, which is sutured behind it, and place it between the muscles and the skin. The skin is sutured in the usual way. This method has in view subsequent surface irradiation. Two weeks after operation, if the wound is soundly healed, a Columbia paste plaque 15 mm thick is made ; it covers the upper half of the abdomen and carries 60 to 80 mg of radium in small needles uniformly distributed over the whole surface of the plaque.

The apparatus is worn from twelve to fourteen hours daily for two weeks

ILLUSTRATIVE CASE

Mrs. J. age forty years. When first seen she had a hard palpable tumour in the epigastrium. There were numerous cutaneous deposits around the umbilicus forming a hard plaque the size of a silver dollar. Vomiting was persistent with progressive loss of weight. No glands were palpable in the supra-umbilical regions. There was no free fluid in the peritoneum and the liver was not enlarged. A bismuth meal showed a large filling defect in the pyloric half of the stomach.

The patient was operated upon by the author at the Radium Institute, London. A transverse incision was made in the epigastrium well above the cutaneous periumbilical deposit. The pylorus was found to be the seat of an extensive neoplasm and hard masses of glands were present along both curvatures. The round ligament was infiltrated with malignant disease and the area of the umbilicus was involved to a slightly lesser degree than the corresponding area of the skin. No secondary deposits were found in the liver. An anterior gastrojejunostomy was performed and twenty three radon seeds distributed along both curvatures and in the lesser omentum (Fig. 43).

The abdomen was closed. Recovery was uneventful. Ten days after irradiation surface application by means of a Columbia paste plaque was given the total dose being 10,000 mg. hours in ten days.

At the end of the treatment the cutaneous involvement had completely disappeared and the umbilicus was normal. A tumour was still palpable in the epigastrium. Vomiting ceased completely. The patient was sent to a convalescent home and put on 7 lb. in weight in one month. The after history is as follows. The patient had several attacks of diarrhoea with distension of the abdomen lasting a day or two. Five months after treatment she was admitted to an infirmary with acute intestinal obstruction. No operation was performed as the patient was too ill and she died twenty-four hours later.

A post mortem examination revealed a ruptured cecum but the cause of the obstruction was not found. There were no secondary deposits in the liver. The abdominal wall was normal. The pyloric growth had greatly diminished in size—the pylorus itself being greatly hypertrophied.

Neuman and Coryn¹⁰³ report the following case. The patient was a waiter fifty-three years of age. Subtotal gastrectomy for carcinoma of the pylorus was performed in 1921. Recurrence of symptoms occurred eleven months

after operation ; there was also induration of operation scar. Six months later the general condition of the patient was bad. There was marked loss of weight, and locally a recurrence the size of an orange was present extending from the laparotomy scar and fixed deeply in the peritoneal cavity. Biopsy showed a typical cuboidal-celled carcinoma. Access to the tumour was obtained by an incision on each side of it extending into the sheath of the rectus. Ten needles, each containing 0.6 mg of radium, were inserted into the deeper part of the growth and fifteen needles of 1.25 mg each into the superficial part. They were left in position six days. Total dose 28.8 M C D. The patient left the Radium Institute twelve days after admission. When seen five months later the tumour had totally disappeared, general health had improved, and the patient had resumed work as a waiter. Nine months after irradiation there was rapid local recurrence and death.

The authors emphasise the importance of the case, which demonstrates the possibility of needling an inoperable carcinoma of the stomach when the growth is isolated by adhesions from the general peritoneal cavity.

Calien¹⁰⁶ reported to the Société Belge de Chirurgie the following case —

Carcinoma of the stomach involving the greater curvature and greater part of the stomach and implicating the glands along both curvatures. Marked filling defect shown in skiagram. Transverse laparotomy was performed and the tumour fixed to the abdominal wall and covered only by skin. Surface application by Columbia paste 2 mm thick, carrying seventeen tubes of radium (ten tubes screened with 2 mm of platinum and seven tubes screened by 1 mm of platinum were applied). Total dose 129 M C D in fourteen days.

Three months after treatment the patient had put on 24 kg in weight, the general health had improved and the skiagram showed nearly total disappearance of the filling defect. Recurrence occurred a few months later, and a second surface irradiation was given. Ninety mg of radium

(nine tubes at 10 mg each, 2 mm of platinum screenage) were applied 6 cm from the skin for nineteen days. Total dose 260 MCD. Recovery followed. The patient was alive and working at the time of publication (1925).

Cahen's case shows (1) The possibility of surface treatment after extra-peritonealisation of the stomach. (2) The possibility of repeating the treatment, the dosage being greatly increased at the second application.

Improvements of technique up till now have led to the adoption of radon seeds in the treatment of gastric cancer, and to the combination of interstitial with surface therapy. Temporary disappearance of the primary tumour, secondary deposits and recurrences has been achieved and life prolonged. With distance therapy and much larger quantities of radium better results may be anticipated.

REFERENCES

- 96 BERARD L and SARGON, A. Cancer de l'œsophage. Paris (Doin 1926)
- 97 LEDOUX L and STUYS. Technique de localisation des Cancers de l'œsophage. *Journal de Rad et d'Electrol*, Vol VII, No 12 1923 p 549
- 98 GUISEZ J. Malignant Tumours of the Oesophagus. *Journal Laryngol and Otolary* April 1925 p 228
- 99 RENNERT, E. Ueber Zwei Fälle von Radium nekrosen des Myocards. *Le Cancer* 1927 pp 431-441
- 100 DE NABIAS S. Traitement par le radium de quelques neoplasmes. Chahine Paris 1928 p 76
- 101 MUIR J. Radium Implantation in Oesophagus Cancer. *Laryngoscope* 1927 37 p 660
- 102 HERRINGMAN F R. Malignancy of the Larynx and Oesophagus treated by Radium Emanation. *Laryngoscope* 1927 37 p 664
- 103 WARING Sir H J. The Surgical Treatment of Malignant Disease. Oxf Med Publ 1928 p 85
- 104 BALFOUR D C and HARCIS L H. Cancer of the Stomach. *Collec Papers Mayo Clinic* Vol XXVIII 1926 p 99
- 105 NEUMAN and CORYN. Recidive de cancer de l'estomac traite par l'aiguillage radifere. *Le Cancer* 1923 No 1 p 87
- 106 CAHEN. Cancer de l'Estomac. *Le Cancer* 1925 No 1 p 43

after operation: there was also induration of operation scar. Six months later the general condition of the patient was bad. There was marked loss of weight, and locally a recurrence the size of an orange was present extending from the laparotomy scar and fixed deeply in the peritoneal cavity. Biopsy showed a typical cuboidal-celled carcinoma. Access to the tumour was obtained by an incision on each side of it extending into the sheath of the rectus. Ten needles, each containing 0.6 mg. of radium, were inserted into the deeper part of the growth and fifteen needles of 1.25 mg. each into the superficial part. They were left in position six days. Total dose: 25.8 M.C.D. The patient left the Radium Institute twelve days after admission. When seen five months later the tumour had totally disappeared, general health had improved, and the patient had resumed work as a waiter. Nine months after irradiation there was rapid local recurrence and death.

The authors emphasise the importance of the case, which demonstrates the possibility of needling an inoperable carcinoma of the stomach when the growth is isolated by adhesions from the general peritoneal cavity.

Cahen¹⁰⁵ reported to the Société Belge de Chirurgie the following case:—

Carcinoma of the stomach involving the greater curvature and greater part of the stomach and implicating the glands along both curvatures. Marked filling defect shown in skiagram. Transverse laparotomy was performed and the tumour fixed to the abdominal wall and covered only by skin. Surface application by Columbia paste 2 mm. thick, carrying seventeen tubes of radium (ten tubes screened with 2 mm. of platinum and seven tubes screened by 1 mm. of platinum were applied). Total dose: 129 M.C.D. in fourteen days.

Three months after treatment the patient had put on 24 kg. in weight, the general health had improved and the skiagram showed nearly total disappearance of the filling defect. Recurrence occurred a few months later, and a second surface irradiation was given. Ninety mg. of radium

(nine tubes at 10 mg each, 2 mm of platinum screenage) were applied 6 cm from the skin for nineteen days. Total dose 260 MCD. Recovery followed. The patient was alive and working at the time of publication (1925).

Cahen's case shows (1) The possibility of surface treatment after extra peritonealisation of the stomach. (2) The possibility of repeating the treatment, the dosage being greatly increased at the second application.

Improvements of technique up till now have led to the adoption of radon seeds in the treatment of gastric cancer and to the combination of interstitial with surface therapy. Temporary disappearance of the primary tumour, secondary deposits and recurrences has been achieved and life prolonged. With distance therapy and much larger quantities of radium better results may be anticipated.

REFERENCES

- 96 BERARD L. and SARGON V. Cancer de l'œsophage. Paris (Doin 1926)
- 97 LEEDLY L. and SLUYS. Technique de localisation des Cancers de l'œsophage. *Journal de Rad et d'Electrolog* Vol VII No 12 19-3 p 549
- 98 GLI EZ J. Malignant Tumours of the Œsophagus. *Journal Laryngol and Otolary* April 1925 p 228
- 99 RENFERN E. Ueber Zwei Falle von Radium nekrosen des Myocards. *Le Cancer* 19-7 pp 431-441
- 100 DE VABIAS S. Traitement par le radium de quelques neoplasmes. Chahine Paris 19-8 p 76
- 101 MUIR J. Radium Implantation in Œsophagus Cancer. *Laryngoscope* 19-7 37 p 660
- 102 HERRIMAN F R. Malignancy of the Larynx and Œsophagus treated by Radium Emanation. *Laryngoscope* 1927 376 p 664
- 103 WARING Sir H J. The Surgical Treatment of Malignant Disease. *Oxf Med Publ* 19-8 p 85
- 104 BALFOUR D C and HARGIS E H. Cancer of the Stomach. *Collec Papers Mayo Clinic* Vol XVIII 1926 p 99
- 105 NEUMAN and CORYN. Recidive de cancer de l'estomac traite par l'aiguillage radifere. *Le Cancer* 1923 No 1 p 87
- 106 CAHEN. Cancer de l'Estomac. *Le Cancer* 1925 No 1 p 43

CHAPTER XII

CARCINOMA OF THE LUNGS

WITH the exception of a short chapter in de Nabias' ¹⁰⁷ book, no report of radium therapy of cancer of the lung is to be found in the literature. This is remarkable if the marked increase of the disease in recent years is taken into consideration. In a leading article in the *Lancet* of July 16th, 1927, the following statement is made: "During the last four or five years several pathologists in Europe and America have drawn attention to the fact that cancer of the lung has become substantially more frequent in their experience than it used to be." As regards operability of these tumours, Tudor Edwards ¹⁰⁸ states: "At present malignant disease arising in the chest—mediastinum, pleura or lung—unfortunately rarely offers any hope of radical operation. This results from two factors: the first, that as a rule it commences insidiously and until extension to surrounding structures, such as pleura or bronchi, occurs there are no localising symptoms, the general symptoms of lassitude and loss of weight alone being present. Therefore, at the time when diagnosis is possible, the growth is too extensive for any radical operation. The second factor is the site of origin of malignant disease. In the vast majority of cases the start is in the mediastinum in close relationship with vital organs or the structures in the hilum of the lung, where it would entail, at least, complete unilateral pneumectomy before there could be any hope of eradicating the disease."

The tumours of the lungs may be primary or secondary to malignant disease elsewhere. If primary, the neoplasm may be either a sarcoma or a carcinoma, the latter is by far the commoner. It may be infiltrating in type and hard or of the soft, rapidly-growing variety. Histologically the

structure of the growths varies with the site of origin, and may be cuboidal-celled or columnar-celled Waring ¹⁰⁹ states that metaplasia may take place and the carcinoma become squamous-celled According to Kerley ¹¹⁰ it arises most frequently from a main bronchus near the bifurcation of the trachea, but may also have its origin in a small bronchus or in the centre of the lung From the lung the growth extends to the lymphatic glands, thoracic viscera, and in some cases to the dorsal vertebrae Harry L Parker ¹¹¹ reports four cases of primary carcinoma of the lung with involvement of the central nervous system by metastasis, in his cases the primary growth gave few local symptoms

X-ray examinations are of great importance, and help not only in the diagnosis but also in the localisation of the disease Kerley ¹¹⁰ has made an extensive study of this subject and maintains that in the X-ray diagnosis of intra-thoracic conditions it is possible to associate certain definite appearances with the presence of malignant disease In considering treatment, malignant disease of the lung may be classified in three clinical stages —

(1) Stage of onset of the disease, characterised by an increase of the respiratory rate, expectoration and cough
(2) Stage of full development of the disease, characterised by dyspnoea, small hæmoptysis and pain
(3) Terminal stage of the disease This classification which is arbitrary, and lacks not only in accuracy but also in definition has perhaps one useful point to recommend it—namely that surgical treatment is only practicable in the first stage, and radium therapy cannot be expected to be of any avail in the third stage The second group is that most commonly met with, owing to difficulty in diagnosis in the early stages In attempting to develop a technique of irradiation, the following points must be taken into consideration —

(1) The disease is difficult to diagnose early, when surgical treatment might be of value Generally when a correct diagnosis is possible the case is not operable

(2) The histology of these tumours shows them to belong

to the group of cuboidal or columnar-celled carcinoma. From experience in radium therapy in other situations, it is known that this type of tumour is less radiosensitive than the squamous-celled carcinoma and requires prolonged irradiation.

(3) The disease is diffuse and efficient interstitial irradiation is difficult to obtain.

(4) The presence of cartilage in the larger bronchi necessitates full platinum protection.

(5) Interstitial irradiation needs a good exposure of the tumour—this may not be possible owing to the presence of adhesions.

The method of irradiation which is likely to be successful is surface or distance application, it presents the following advantages :—

(1) A large quantity of radium can be used.

(2) The treatment can be prolonged over a sufficiently long period of time

(3) Several ports of entry are available.

(4) Surgical risks are eliminated

Technique

The exact position and extent of the lesion are ascertained by radiological methods. If a pleural effusion is present it is aspirated in one or more sittings, but is not replaced by air. Aspiration is repeated during the treatment. A layer of fluid between the source of irradiation and the tumour diminishes the effect of the irradiation. An extensive plaque of Columbia paste 15 mm thick is prepared. The plaque covers the whole of the affected side of the chest and extends beyond the middle line in front and up to the middle line behind. It covers the anterior part of the chest, the axilla, the supraclavicular area, the side and back of the thorax. When completed the wax model is divided in two parts along the midaxillary line. 75 to 100 mg of radium in numerous small foci are distributed equally over the plaque or in between two layers of adhesive plaster. Irradiation is alternatively

anterior and posterior, the adhesive plaster containing radium being transferred from one part of the wax plaque to the other. Eighteen to twenty hours daily are given in all, half on each aspect. Treatment is prolonged for twenty-one to twenty-five days. By this method the skin receives one half or one-third of the total dose given. The average total dose varies from 40,000 to 50,000 mg hours.

Improvement of the patient's condition is noticeable after the tenth to twelfth day. Pain is eliminated, dyspnoea is lessened and expectoration diminishes. Occasionally rises of temperature occur, this is not an indication for the cessation of treatment, it is due to the changes in the tumour produced by radium and occurs in the treatment of other types of neoplasms. X-ray examination during and after treatment at frequent intervals is both instructive and interesting. As cure or inhibition of the disease means fibrosis to a certain extent these changes are registered in the skiagrams.

It is too early to speak of any but initial results, but these are encouraging. It is justifiable to bring to the notice of clinicians the possibilities of radium treatment of cancer of the lung as the disease is definitely increasing in its frequency and any other form of treatment is at present applicable to a very small proportion of cases. Robert Hutchison¹¹ in a paper read at the Cancer Conference, London, states "There can be no doubt that the experience of the London Hospital confirms that elsewhere in showing that there has been a marked increase in recent years in cases of primary carcinoma of the lung not only absolutely, but relatively to carcinoma in general."

Ralston Paterson¹¹³ in a study of reported cases treated by irradiation, states that all the cases treated by X-rays (nineteen patients) died. Only one apparent success was a case of a small malignant hæmangioma of the bronchus, removed by bronchoscopy and treated by interstitial implantation of radium followed by X-rays. With the development of distance therapy by means of a 'bomb

which permits accurate focussing of the various parts of the tumour, better success may be anticipated

REFERENCES

- 107 DI NABIAS, S "Le traitement par le Radium de quelques neoplasms," p 229
- 108 TUDOR EDWARDS, A "Intrathoracic New Growths · An Account of seven Operable Cases" *Br J S*, Vol XIV, 1927, p 607
- 109 WARING, Sir II J "The Surgical Treatment of Malignant Disease," p 620
- 110 KIRLEY, P "Primary Carcinoma of the Lung with Special Reference to X-ray Diagnosis" *The Cancer Review*, May, 1928, p 195
- 111 PARKER, II L "Involvement of the Central Nervous System in Cases of Primary Carcinoma of the Lung" *Arch Neurol and Psych*, 1927, 17, pp 198-213, and *Mayo Clinic Reports*, 1926, Vol XXVIII, p 1002.
- 112 HUTCHISON, R "The Alleged Increased Frequency of Primary Carcinoma of the Lung." *Rep Internat Conf Cancer*, London, 1928, p 389
- 113 PAIRSON, R "Roentgen-ray Treatment of Primary Carcinoma of the Lung" *Coll Papers of the Mayo Clinic*, 1927, Vol XIX, p 989

CHAPTER XIII

CENTRAL NERVOUS SYSTEM

THE term "cerebral tumour" is used here to denote "Neoplasms" of the brain and meninges. Cysts are included in this group. True tumours of the brain tissue are gliomata. They are nearly always diffuse, degenerative changes are frequently present, and lead to cyst formation. Adenomata and adeno-carcinomata are found in the pituitary gland. Endothelioma are tumours of the membranes, they destroy the skull by pressure atrophy and are accompanied by new bone formation. From the surgical aspect they are best classified into *intra-neural* and *extra-neural* tumours. Complete surgical removal is possible in the extra-neural varieties owing to the presence of a capsule, or at least to clearly defined limitation. The removal of intra-neural neoplasms is very rarely possible. Surgery of brain neoplasms gives, now and then, brilliant results, in the majority of cases failures are recorded. Decompression operations give palliative results which prolong life, arrest failure of vision and give relief from symptoms. The vast majority of neurological surgery is in the end reduced to the benefits of decompression.

To the neurological surgeon removal of the tumour is the ideal aimed at, Sir Percy Sargent¹¹⁴ in a recent publication, states "A glioma can rarely be removed with the same completeness as an endothelioma. This, however, should not deter the surgeon from making as determined an attack upon a favourable glioma as the circumstances warrant, having regard always to the function of that part of the brain which is involved."

Sir James Purves-Stewart¹¹⁵ concludes his book on 'Intracranial Tumours' with the following remarks

While I yield to no one in my admiration and respect

for the dexterity of our surgical colleagues, I cannot help feeling (and I am sure they realise too) that many cerebral operations are hazardous, crude and mutilating. Under present-day conditions, this is inevitable, even at the hands of the most skilful operator. Let us hope that the time will arrive when many surgical operations on the brain, as on other organs, will be discarded in favour of other more efficient and gentler methods, biochemical or physical, whereby we shall be able to melt away growths, no matter how deeply seated or how insidiously infiltrating, or better still, when we may succeed in raising the resistance of the body so as to prevent their appearance altogether."

The basis of radium treatment of cerebral tumours is the difference of sensibility to irradiation presented by normal brain tissue and the tumour. Nervous tissue, both grey matter and white, is highly radio-resistant, it is true that experimentally radionecrosis of cerebral substance can be produced, but the doses given are well beyond the range of clinical application of radium therapy, the lesion in these cases is purely caustic, and the result is destruction of living tissues irrespective of their histological structure. Within the limits of the clinical dosage it is found that healthy cerebral substance is radio-resistant, whereas neoplasms are very sensitive to gamma irradiation and X-rays. Of the various neoplasms, gliomata are the most sensitive, adeno-carcinomata come next and the most resistant are endotheliomata, specially if they are accompanied by bone formation.

The question of curability of cerebral neoplasms by radium depends upon (1) The extent of the disease (2) The nature of the tumour. (3) The degree of relief given by previous decompression.

CEREBRAL AND CEREBELLAR TUMOURS

Treatment

In this, as in other situations, early diagnosis will greatly facilitate treatment. The bigger the mass to be destroyed by radium the worse the prognosis, secondary vascular

changes in the surrounding normal tissue and presence of oedema affect adversely the results of irradiation

Decompression

Preliminary decompression is an essential step of the treatment. It gives the patient relief from increased intracranial pressure, a window is created through which the underlying tumour is irradiated without the screenage offered by the bone, the risk of osteo-necrosis is eliminated, if a cyst is present it can be removed or aspirated, a biopsy of the tumour becomes possible

Irradiation

Needling of the tumour has been tried by Frazier and Pancoast¹¹⁶. This method, however, presents the following disadvantages: the necessity of drainage of the wound, the difficulty of retuning the needles in position in soft tissues, the presence of a number of platinum needles which together have a considerable volume, uniform irradiation is difficult to obtain, the time factor is limited. Surface irradiation overcomes these difficulties, treatment can be prolonged over a period of weeks, intensity of irradiation can be increased beyond that possible by the interstitial method

Technique

A week after decompression and when the wound is healed, a helmet or cap of Columbia paste is made. It is made to cover at least half of the cranium. The trephine opening is marked on the surface of the cap. Platinum tubes containing 10 mg of radium screened by 0.8 mm of platinum are placed on the wax over the trephine area. Needles containing 1, 1.3 and 2 mg of radium screened by 0.65 mm of platinum are placed outside the trephine area. A total of 50 to 80 mg of radium is used. It is worn continuously or intermittently for eighteen hours daily. The treatment is prolonged over two or three weeks. Average total dose 18,000 mg hours (Fig. 44)

PITUITARY TUMOURS

Pituitary tumours are adenomata or adeno-carcinomata. From their peculiar anatomical situation, their growth is hampered by the dura and bone. Extension which at first is intraglandular, soon stretches the capsule of the gland and presses both upon the optic chiasma and on the floor of the sella turcica; the bone undergoes pressure atrophy and the tumour may bulge with the thinned sella

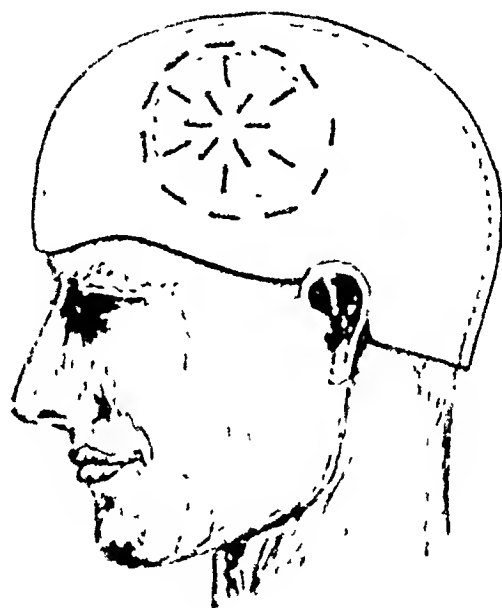


FIG. 44

FIG. 44. Pituitary tumour, showing extension of tumour into the sphenoidal sinus.

into the sphenoidal sinus. With upward extension the tumour soon reaches the limits of the diaphragma sellae and obtains more freedom for itself in the cranial cavity, extending up on the third ventricle and causing internal hydrocephalus.

In 1905, 5 per cent. of pituitary tumour under the name of *Pituitary Cellaroma*,¹¹⁷ Dorr and Bailey¹¹⁸ classify the tumours into three histological groups—the chromophilous type, the chromophiladenoma, and the basophilous type.

The chromophilous type, popularly of the *adenoma* type, is

spreads and invades surrounding structures and in some cases gives rise to metastasis

Diagnosis of pituitary tumours is based upon (1) Ophthalmological examination which reveals optic atrophy and typical changes in the visual fields (2) X-ray evidence of changes in the sella turcica (3) Signs of intracranial tension due to internal hydrocephalus (4) Changes due to defects in internal secretion of the gland

Surgical treatment aims at relief of intracranial pressure and preservation of vision. The gravity of the operation is justified if the natural course of events is taken into consideration. Mortality, even in the hands of the exceptionally skilful surgeon accustomed to neurological surgery, is high. Sargent¹¹⁸ in sixty-eight cases of operation for supposed pituitary tumour, quotes a mortality of thirteen cases (19.1 per cent). In thirty-three cases of pituitary tumour proper, there were nine deaths (27 per cent). Cushing's¹¹⁷ series of 162 cases shows 8.6 per cent mortality in the transphenoidal route and 5.2 per cent in the transfrontal route. Statistics, however, are not an absolute indication of the value of the operation if vision is saved. In the consideration of the surgical treatment of hypophyseal tumours another factor is to be remembered, complete removal of the tumour is rarely, if ever, possible.

Preservation of vision and relief from intolerable headache are usually achieved by surgical means.

Can radium show similar results, and if so, is the mortality of radium therapy less than of surgical removal?

Radium Treatment

The introduction of radon seeds into the tumour either by the frontal operation or by the nasal route was tried by Pancoast in 1922¹¹⁶—the results were not very good chiefly owing to absence of suitable screenage and also from the additional factor of a surgical risk as great as in the operation for removal of the tumour. With increased knowledge of radium therapy better results can be anticipated. The introduction of screened platinum seeds

into the tumour presents the disadvantages that all seed tend to fall by gravity on the floor of sella tureica and uniform irradiation is not obtained, and the risk of necrosis is still present. The removable seed or, better still, the removable needle, has many advantages. Roek Carling has devised a radium needle of small size, well screened by platinum, attached to a celluloid peg and provided with an eye at the distal end (Fig. 2).

Celluloid pegs of suitable lengths can be screwed on to the miniature radium needle. Each needle contains 0.5 mg. of radium screened by 0.5 mm. of platinum.

In the proposed method the distance between the tumour and the surface is ascertained by means of radiography. The suitable route of approach is chosen in each individual case. In the sphenoid type, the nasal route is adopted, in the suprasellar type the frontal route. A minute trephine hole is made in the frontal area; a trocar and canula are passed along the floor of the anterior fossa into the tumour, gentle aspiration is made to evacuate the contents of a cyst; the needle with ivory peg is introduced into the canula, which is then withdrawn. The position of the needle is controlled by radiograms. The needle is left in position seven days. This method of treatment is at present being tried by Roek Carling and the author. It aims at an accurate irradiation with a minimum surgical risk, it is an improvement on the seed implantation method, and presents advantages over X-ray treatment as the latter is of very little avail in cysts or carcinomata, although it gives very good results in cases of adenomata of the pituitary.

TUMOURS OF THE SPINAL CORD

Tumours of the spinal cord may be primary or secondary deposits from a malignant growth elsewhere. In all cases they demand a laminectomy. If the tumour is intrathecal, but extra-medullary, it is as a rule benign and removable. Intramedullary tumours are irremovable. Extrathecal tumours may be removable or irremovable according to their structure and extent. Laminectomy is an essential

step in the treatment. If the tumour is found to be irremovable, surface irradiation is resorted to. When the operation wound is healed a Columbia paste plaque 15 mm thick is moulded over the operation area and 50 to 75 mg of radium are placed along the midline of the spine and on each side of it. The plaque is worn sixteen to eighteen hours daily for fourteen days. As the area treated is not extensive and the intensity of irradiation appreciable peeling of the skin is unavoidable if an adequate dose is to be given. The results are encouraging and return of function may be anticipated.

Another method of treatment is the insertion into the laminectomy wound of a sterile wax model accurately fitting into the space created by the removal of laminae and spinous processes. The model is applied so as not to press on the cord. It contains 30 mg of radium in small needles and is left in position seven days.

ILLUSTRATIVE CASES

Mrs G. A. age thirty four years. (Left prefrontal neoplasm) Under the care of Sir James Purves Stewart. In good health till April 1926 when patient had intense headache and vomiting for one day. In May and again in April there was a sudden momentary blindness with subsequent gradual deterioration of vision. In September 1926 dragging of right leg and optic neuritis. In February 1927 slight right sided hemiparesis and commencement of optic atrophy of both discs. Intense headache. In May 1927 a pneumoradiogram showed both lateral ventricles displaced to the right. On May 17th 1927 vomiting and convulsions starting in the right upper limb. Loss of consciousness. The patient had twelve fits in three hours. Left frontal decompression was done by Mr Arthur Evans. Recovery of consciousness but right sided convulsions continued for several days. On June 1st the patient was much worse. There was right sided weakness, aphasia, incontinence and marked bulging of the brain. Fifty mg of radium were applied on a Columbia paste helmet (five tubes at 10 mg each 0.8 mm of platinum and 1 mm of copper). Continuous application the first twenty four hours followed by twelve hours daily. Four days later the patient could speak and walk without assistance. On June 7th speech and articulation were normal. No weakness of legs but unsteady gait. Knee jerks and ankle jerks normal and equal. Radium removed on the tenth day. Total dose 6,600 mg hours. Peeling of forehead and loss of hair followed irradiation. On

June 21st there was a well-marked hernia cerebri indicative of persistent intracranial pressure (Fig. 45). On July 23rd, 1927, the left frontal lobe was again explored by Mr. Arthur Evans in its anterior half, but no circumscribed growth could be palpated and the wound was again closed. Following this last operation the right-sided fits ceased and her only abnormal physical signs were pallor of the optic discs, with vision in the left eye reduced to perception of light; in the right eye vision, as tested by Mr. MacCallan, was 6/6. The pupils and cranial nerves were otherwise normal, save for flattening of the right naso-labial fold on emotional movement. There was no motor abnormality of the limbs. The supinator-jerks, knee-jerks



FIG. 45 —PATIENT OF SIR JAMES PURVES-STEWART

Case of left prefrontal neoplasm. Well-marked hernia cerebri indicative of persistent intracranial pressure after decompression.

and ankle-jerks were normal and equal. The right plantar reflex was indefinite, the left was flexor. The abdominal reflexes were present and equal on both sides. Meanwhile the hernia cerebri, although still present, was definitely smaller and no longer tense, but flaccid on palpation. On October 31st, 1928, the patient wrote: "I am quite well, and up to the present I have had no trouble since I left Westminster Hospital." She leads a normal life and looks after her household duties. The patient was re-examined by Sir James Purves-Stewart on November 16th, 1928 (sixteen months after the radium application), the operation gap was now concave (Fig. 46), pulsating with the heart and giving an impulse on coughing. She has had no more fits or other discomfort. The physical signs were

exactly as before. Vision in the left eye was reduced to perception of light in the right eye it was normal. There was slight weakness of the right lower face on emotional movement. Otherwise no sensory motor or reflex abnormality could be detected.

Miss P. S. aged eighteen. Case under the care of Mr. Tudor Edwards. In July, 1927 excision of sarcoma of lung. In January, 1928 laminectomy for secondary deposit in the spine and vertebral column at the level of the 6th to 8th dorsal vertebrae. In July



FIG. 46

The same patient as in Fig. 45. Sixteen months after radium treatment. The operation area is concave.

1928 the patient was bedridden, unable to move her legs. There was a swelling to the left of vertebral column at the level of the laminectomy. Fifty mg. of radium in 50 foci applied on Columbia paste 15 mm. thick over the swelling eighteen hours daily for twelve days. Total dose 9,900 mg. hours. Marked peeling of skin. Distinct improvement noticed soon after cessation of treatment. The swelling in the dorsal region became smaller gradually with return of power in both legs. On August 8th 1928 the patient could walk unaided. Although subsequently the patient's general health deteriorated owing to recurrences and death ensued the disappearance of the tumour and return of function after irradiation are noteworthy.

Post-operative irradiation of the glandular area involved is carried out on the lines indicated in Chapter V.

RODENT ULCER

Unless involving bone, this type of neoplasm responds well to radium in the majority of cases. The good results,



FIG 47

Skigram of needles around the periphery and in the centre of an epithelioma of the skin shown in Plate XIII, A

however, although in the majority, are not universal, and some rodent ulcers are radio-resistant. It is impossible, clinically, to distinguish those which respond well to radium treatment from the others. Histologically and microscopically, there is no distinguishing feature on which to base a prognosis. Good results are obtained by the use of β and γ irradiation for short periods. The method employed by the author is to use large quantities of well-screened radium for short periods of time

PLATE XIII

Epithelioma of Thigh

A Before treatment

B Two months after treatment



A



B



The treatment is repeated until the ulcer is healed.

Technique

50 to 100 mg of radium are applied to the surface of the lesion. Columbia paste is used for this purpose, being placed directly in contact with the lesion and left in position two hours. At the end of this time there is a definite change in the appearance of the lesion which is flatter and smaller. After the paste is removed desloughing forms and healing takes place undisturbed. At the end of a month or six weeks the lesion is healed.

An alternative method is to make a plug of Columbia paste or stent lined with lead. A hole is cut in the plaque and this is made to correspond to the lesion. 50 to 40 mg of radium are applied on the surface of the plaque and maintained in position by strapping. The whole apparatus is applied accurately to the lesion and left in position forty-eight hours.

ILLUSTRATIVE CASE

Mrs C, age seventy. Epithelioma on anterior aspect of left thigh, ulcer 4 in by 5 in. Enlarged glands in groin (Plate XIII).

Treatment—Interstitial irradiation (Fig. 47) and surface application by means of Columbia paste. Total dose 10,000 mg hours. The ulcer healed slowly and the condition two months after treatment is shown in Plate XIII.

CHAPTER XV

SARCOMA

MALIGNANT tumours of connective tissue origin may be divided for the purpose of treatment into : (1) Lymphosarcoma ; (2) Chondrosarcoma ; (3) Osteo-sarcoma , (4) Sarcoma of muscle

Lymphosarcoma

This type of tumour is extremely sensitive to radium treatment Large masses of tissue can be made to disap-



FIG 48

Patient under the care of Mr Arthur Evans and the author Lympho-sarcoma Condition before treatment

pear in a very brief period of time (Figs 48 and 49) They require small doses as compared to other types of sarcoma The disappearance of the tumour is a purely local reaction, and in no way affects the development of metastatic tumours

elsewhere, these are equally susceptible to treatment. Local recurrences are more radio-resistant, and it is noticed that irradiation in some cases makes the patient resistant to further radium treatment.

The commonest situation of lymphosarcoma is the cervical area and the retroperitoneal space. Both situations are treated by means of Columbia paste plaques carrying relatively small doses of radium. For the cervical area 25 to 40 mg. in numerous needles of 0.6 and 1.3 mg. of

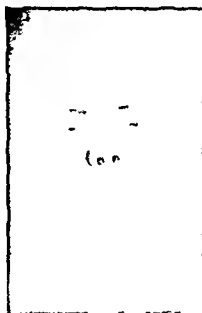


Fig. 4)

The same patient as in Fig. 45. The day after completion of treatment. Rapid disappearance of the knot treated.

radium are distributed over the surface of the plaque. They are left in position four to six days. A total dose of 10,000 mg. hours is as a rule sufficient. For the tonsil interstitial irradiation by means of seeds is carried out. For the retroperitoneal sarcoma surface application by means of anterior and posterior plates is done. The area to be treated is large and requires 75 to 100 mg. of radium, this is distributed over both plaques, they are left in position seven to twelve days. Average total dose 20,000 mg. hours.

Chondrosarcoma

This is a suitable type for radium treatment. If the tumour is voluminous interstitial irradiation with very small quantities of radium (8 to 10 mg. in four to six needles) gives good results. Laborde ¹¹⁹ reports the case of a man with an enormous sarcoma in the region of the scapula. This tumour had been previously treated with deep therapy X-rays without effect. 8 mg. of radium were inserted in the tumour, which melted in four days. Chondrosarcomata of the ribs, clavicle, sternum, have been successfully treated with radium. Roy Ward ¹²⁰ reports a case of sarcoma of the clavicle treated in 1913 and reported well fourteen years later.

Osteo-sarcoma

Sarcomata of long bones are radio-resistant, and results of radium therapy are very rarely successful.

Sarcomata of the bones of the face are more suitable for radium treatment. The writer has treated at the Radium Institute a patient with a sarcoma of the left malar bone and zygoma rapidly recurring after excision. The patient was four months pregnant. On the advice of Mr. Hayward Pinch interstitial irradiation with large quantities of radium for a short time was given, and this was followed by complete disappearance of the growth. Pregnancy proceeded to full term, and the patient is reported by her doctor to be well eight months after treatment.

Sarcoma of Muscle

Localised sarcoma of a muscle or intermuscular septa belong to the group of fibro-sarcomata or recurrent fibroma. The results of radium treatment are good. The combination of surgery with post-operative irradiation gives a better prognosis than surgery alone.

Roy Ward ¹²⁰ gives an account of thirty cases of inoperable sarcomata treated with radium, of the total twelve present no evidence of disease for periods varying from

fourteen years to seven months after treatment, ten died, five are improved, three derived no benefit. He states that "relief of symptoms and prolongation of life are seen in most cases, and some patients remain in good health for long periods, the growth becoming shrunken and fibrosed."

ILLUSTRATIVE CASES

Mr M age nineteen Lymphosarcoma of neck, four months history. Fig 48 shows the condition before treatment. 40 mg of radium were applied on the left side of the neck by means of a Columbia paste collar twelve hours daily for seven days. Total dose 3 360 mg. The swelling disappeared entirely in one week. Fig 49 shows the condition five days after cessation of treatment. The patient died three months later from recurrence in the liver, spleen and general dissemination.

Mr W F age twenty eight Tumour the size of a tangerine orange in the left vastus internus muscle.

Biopsy—Fibro sarcoma

Treatment—Excision of tumour followed by interstitial irradiation with fourteen needles of 0.6 mg of radium element each. Total dose 216 mg hours. surface application at a distance of 4 cm. 40 mg for twenty eight hours. Total dose 1 120 mg hours. Well three years.

REFERENCES

- 119 LABORDE S. *La Curiothérapie des Cancers* p 272
120 WARD ROY. Inoperable Sarcomata treated with Radium
BMJ January 25th 1928

CHAPTER XVI

PROTECTION OF RADIUM WORKERS

THE necessity of protection of the personnel engaged in radium therapy is well known. Small doses of gamma rays are received by those threading and cleaning needles and tubes and by the surgeon and his assistants, implanting radium needles or preparing Columbia paste casts. To prevent any possible local reaction it should be a rule never to touch radium needles with bare hands; forceps 10 cm. long should be used; the radium when taken to the operating theatre should be kept in a small lead-lined safe and only taken out immediately before use. When not in use radium should be kept in a safe filled with lead composed of a number of tubular units, the central portion only being used as a repository for radium. For transport a small lead-lined box with a long handle should be used.

Manipulation of Columbia paste plaques should be done with thick lead-lined rubber gloves. The efficiency of the gloves can be tested by placing on the inside of the glove over the palm of the hand a small film (a dental X-ray film) and testing it at the end of a week, or less if frequent manipulation has been necessary. In the wards where radium cases are nursed, the nursing staff should be changed at frequent intervals. The possibility of a hæmic reaction should not be forgotten, and blood counts should be done either as a routine or at the first sign of ill-health. It is possible to work constantly in an institution where radium therapy is practised without any ill effects to the personnel.

Anatomy Physiology Biochemistry

Surgical Anatomy. By GRANT MASSIE, F.R.C.S. 121
Illustrations, some in colour 15s net

Recent Advances in Anatomy. By H. WOOLLARD,
M.D. 4 Coloured Plates and 73 Text figures 12s 6d net

The Principles of Anatomy as Seen in the Hand.
By F. WOOD JONES, D.Sc., F.R.S. 125 Illustrations 15s net.

The Anatomy of the Human Skeleton. By J. ERNEST
FRAYER, F.R.C.S. 2nd Edition 219 Illustrations, many in Colours. 28s. net

Synopsis of Anatomy. By T. B. JOHNSTON, M.B., Pro-
fessor of Anatomy, Univ of London 2nd Ed 11 Illus 12s 6d net

The Adrenals: their Physiology, Pathology and
Diseases By MAX A. GOLDBILDER, M.D. 73 Illustrations 30s net

Heath's Practical Anatomy: a Manual of Dissec-
tions Edited by J. E. LANE, F.R.C.S. 9th Edition 321 Engravings 15s net

Clinical Applied Anatomy; or, The Anatomy of
Medicine and Surgery By CHARLES R. BOX, M.D., and W. McADAM
ECCLES, M.S. Lond., F.R.C.S. Eng. 45 Plates 12s 6d net

Essentials of Surface Anatomy. By C. R.
WHITFARER, F.R.C.S. Third Edition With 17 Plates 7s 6d net

Text-Book of Anatomy and Physiology. By
E. R. BUNDY, M.D. 6th Edition With 266 Illustrations 12s net

Starling's Principles of Human Physiology.
Sixth Edition Edited by C. LOVATT EVANS, D.Sc., F.R.C.P., F.R.S.,
Jodrell Professor of Physiology, University College, London 562 Illus-
trations, 10 in colour 24s net

Human Physiology. By F. R. WINTON, M.D., Univer-
sity Lecturer in Physiology, Cambridge, and J. E. BAYLISS, Ph.D.,
Bent Memorial Fellow, Assistant in Physiology, University College,
London 227 Illustrations 15s net

Practical Physiology By G. V. ANREP, M.D., D.Sc.,
and D. T. HARRIS, M.B., B.S. Second Edition Ready Oct, 1933

Synopsis of Physiology. By FRANKCON ROBERTS, M.D.,
M.R.C.P. With 73 Illustrations 10s 6d. net

An Introduction to Biophysics. By D. BURNS,
D.Sc. Second Edition 116 Illustrations 25s net

Recent Advances in Physiology. By C. LOVATT
EVANS, D.Sc., F.R.C.P., F.R.S., Jodrell Professor of Physiology, University
College Fourth Edition 113 Illustrations 12s 6d net

Recent Advances in Biochemistry. By J. PRYDE,
B.Sc., M.Sc. Third Edition 42 Illustrations 12s 6d net

A Text-Book of Biochemistry for Students of
Medicine and Science By A. T. CAMERON, D.Sc., F.I.C., Professor of
Biochemistry, Univ of Manitoba 3rd Edition 2 Plates and 13 Text
figures 15s net

A Course in Practical Biochemistry. By A. T.
CAMERON and F. D. WHYTE, A.R.T.C., Ph.D. Second Edition 4 Plates,
23 Text figures 8s 6d net

The Biochemistry of Medicine. By A. T. CAMERON
and C. R. GILMOUR, M.D., C.M. 31 Illustrations 21s net

Materia Medica Pharmacy

Recent Advances in Materia Medica (Sera, Vaccines, Hormones and Vitamins) By J H BURN M.D. Director of the Pharmacological Laboratories Pharmaceutical Society of Great Britain 2 Illustrations 1s 6d net

Applied Pharmacology By A J CLARK, M.C. M.D., F.R.C.P. Professor of Materia Medica and Pharmacology University of Edinburgh Fourth Edition With 72 Illustrations 17s net

Text-Book of Pharmacology and Therapeutics By A I CUSHNY M.A. M.D. F.R.S. Ninth Edition 73 Illus. 40s net

Materia Medica, Pharmacy, Pharmacology, and Therapeutics By Sir W HALE WHITE M.D. F.R.C.P. Twenty first Edition Based on the 1932 British Pharmacopœia Revised by A H DOUTHWAITE M.D. F.R.C.I. 10s 6d net

Synopsis of Pharmacology By D V COW, M.D. Second Edition Revised by G NORMAN MEERS M.D. With 15 Illustrations 7s 6d net

A Text-Book of Pharmacognosy By H G GREENISH F.R.C. F.L.S. Professor of Pharmaceutics Pharmaceutical Society 6th Edition 297 Illus. 20s net **An Anatomical Atlas of Vegetable Powders** 138 Illus. 17s 6d net

Practical Pharmacognosy By I E WALLIS B.Sc., F.R.C. Second Edition 10 Illustrations 1s 6d net

The Science and Practice of Pharmacy By R P BENNETT B.Sc. F.R.C. and T TESTING COCKING F.R.C. Vol I Pharmaceutical Operations and the Manufacture of Pharmaceutical Substances 160 Illustrations 14s net Vol II The Physical and Chemical Examination of Pharmaceutical Substances 72 Illustrations and Diagrams 15s net

Principles of Pharmacy By H B MACKIE, B.Pharm., Ph.C. 67 Illustrations 10s 6d net

First Lines in Dispensing By H B STEVENS and C F I LECHE A.R.C. F.C.S. Third Edition 90 Illustrations 7s 6d net BY E W LECHE B.Sc. F.R.C. S.M. AND H B STEVENS O.R.C. F.R.C.S.

The Book of Pharmacopœias and Unofficial Formularies 7s 6d net ALSO

The Book of Receipts Twelfth Edition 10s 6d net

The Book of Prescriptions with an Index of Diseases and Remedies Eleventh Edition 10s 6d net

Favourite Prescriptions, Including Dosage Tables etc. Hints for Treatment of Poisoning, and Diet Tables By ESPINE WARD M.D. (1st Edn) Third Edition Interleaved 7s 6d net

Medical and Pharmaceutical Latin for Students of Pharmacy and Medicine By P P BENNETT 7ed Edition 10s 6d net

A Companion to the British Pharmacopœia (1914) By PETER WYATT SQUIRE F.L.S. F.C.S. Nineteenth Edition 2s net **The Pharmacopœias of Thirty One of the London Hospitals** Ninth Edition 12s 6d net

The Pharmaceutical Formulary By HENRY BEASLEY Twelfth Edition by J OLDHAM BRAITHWAITE 6s 6d net

Hygiene

Bacteriology

Recent Advances in Preventive Medicine. By J F C HASLAM, M C, M D, M R C P (Edin), D P H 30 Illustrations 12s 6d net

The Health of the Industrial Worker. By E L. COLLIS, M D, and Major GREENWOOD, F R C P, F R S 38 Illustrations 30s net

The Principles of Preventive Medicine. By R TANNER HEWLETT, M D, F R C P, D P H, and A T NANKIVELL, M D, D P H With 12 Charts and 5 Diagrams 18s net

Synopsis of Hygiene. By W WILSON JAMESON, M A, M D, F R C P, D P H, Professor of Public Health, London University, and Col G S PARKINSON, D S O, M R C S, L R C P, D P H, Assistant Director, Public Health Division, London School of Hygiene and Tropical Medicine Third Edition 20 Illustrations 18s net

A Simple Method of Water Analysis. By J C THRESH, M D, D P H, and J F BEALL, M R C S, D P H Tenth Edition 3s net

Elementary Hygiene for Nurses. By H C R. DARLING, M D, F R C S Fifth Edition 58 Illustrations 5s net

Preservatives in Food and Food Examination. By J C THRESH, D Sc, M D, D P H, and ARTHUR E PORTER, M D, M A Cantab 8 Plates 16s net

Beverages and their Adulteration. By H. W WILEY, M D, Ph D 42 Illustrations 21s net

Text-book of Meat Hygiene. By R EDELMANN, Ph D. Translated by J R MOHLER, A M, V M D, and A EICHHORN, D V S Fifth Edition With 161 Illustrations and 5 Plates 28s net

A Manual of Bacteriology: Medical and Applied. By Prof R T HEWLETT, M D, F R C P, D P H, and Prof J McINTOSH, M D, B Ch Ninth Edition 43 Plates and 66 Text-figures 18s net

Immunity: Methods of Diagnosis and Therapy. By Dr J CITRON Second Edition 40 Illustrations 14s net

Lessons in Disinfection and Sterilisation. By F W ANDREWES, M D, F R C P Second Edition 31 Illustrations 3s 6d net

The Principles of Practical Bacteriology for Scientific Workers By J H JOHNSTON, M Sc, and R H SIMPSON, M D, M R C P 5s net

Medical Bacteriology, including Elementary Helminthology By L E H WHITBY, C V O, M D, B Ch, Assistant Pathologist, Middlesex Hospital 75 Illustrations 10s 6d net

Recent Advances in Bacteriology. By J H DIBLE, M B, F R C P Second Edition 29 Illus 15s net

Dairy Bacteriology. By Dr ORLA-JENSEN Translated by P S ARUP, M Sc, F I C Second Edition 67 Illustrations 18s net

The Examination of Waters and Water Supplies By J C THRESH, D Sc, M D, D P H, J F BEALE, M R C S, L R C P, D P H, and E V SUCKLING, M R C S, L R C P, D P H Fourth Edition 61 Illustrations 42s net

Pathology & Psychology Dictionaries

- Recent Advances in Pathology** By C. HADFIELD M.D. F.R.C.P. and H. I. CARROD M.B. M.R.C.P. 6 Illus. 15s net
- Laboratory Diagnosis, With Clinical Applications for Physicians** By E. F. O'CONNOR M.D. and H. D. HASKIN M.D. of Univ. of Oregon U.S.A. 6 Col. 111st and 112nd At figures 15s net
- Chemical Methods in Clinical Medicine** By G. A. HARRISON M.D. B.Ch. F.R.C.P. 1 vol. in Chemical Pathology in the Univ. of London 2 Colours 111st and 63rd At figures 15s net
- Pathology, General and Special, for Students of Medicine** By I. TANNER HEWLETT M.D. F.R.C.P. D.P.H. Fifth Edition 49 Plates and 112 Text Figures 15s net
- A Handbook of Clinical Chemical Pathology** By F. S. FENWATER M.D. M.Sc. D.I.H. 19 Illus. 5s net
- Clinical Pathology** By P. N. PAXSON M.B. and J. R. MARRACK M.B. 12 Plates (10 Colours) and 101 Text figures 15s net
- A Manual of General or Experimental Pathology** By W. S. FARRER BARLOW M.D. F.R.C.P. Second Edition 15s net The Elements of Pathological Anatomy and Histology for Students 25s net
- Post-mortem Manual** By C. R. BUX M.D. Second Edition 2 Illustrations 10s net
- The Pathologist's Handbook, a Manual for the Post-mortem Room** By I. N. KELYNACK M.D. 12 Illustrations 4s 6d net
- Clinical Lectures on Psychological Medicine** By HENRY YELLOWLEYS O.B.E. M.D. F.R.C.P. 1 vol. 11s net
- Recent Advances in the Study of the Psychoneuroses** By MILLAIS CULLEN M.D. F.R.C.S. Lecturer in Psychoneurosis London Hospital Medical College 4 Illustrations 15s net
- Recent Advances in Psychiatry** By H. DEVINE O.B.E. M.D. F.R.C.P. 4 Illustrations 15s 6d net
- Psychological Medicine** By Sir M. CRAIG M.D. Physician Mental Diseases Guy's Hospital Fourth Edition With the Collaboration of T. BEATON O.B.E. M.D. 25 Illus. 15s net
- The Journal of Mental Science** Published Quarterly by Authority of the Royal Medico-Psychological Association 7s 6d net
- Lang and Meyers' German-English Dictionary of Terms used in Medicine and Allied Sciences** 4th Edition 15s net

Medicine

Medicine : Essentials for Practitioners and Students By G E BEAUMONT, Physician, with Charge of Out patients, Middlesex Hospital 61 Illustrations 21s net

Medical Emergencies. By CHARLES NEWMAN, M D, M R C P, Junior Physician, King's College Hospital 8s 6d net

Taylor's Practice of Medicine. Fourteenth Edition Revised by Drs E P POULTON, C P SYMONDS, H W BARBER and R D GILLESPIE 64 Plates and 103 Figures 25s net

Clinical Atlas of Blood Diseases. By A. PINEY, M.D., and S WARD, M D 2nd Edition 38 Illustrations, 34 in Colour 12s 6d net

ALSO BY DR A PINEY

Recent Advances in Hæmatology. Third Edition 4 Coloured Plates 18 Text figures 12s 6d net

Diseases of the Blood. Second Edition 65 Illustrations, 14 in Colour 18s net

Endocrine Diseases : Their Diagnosis and Treatment By W FALTA (Vienna) Translated by M K MEYERS, M D, with a Foreword by Sir A E GARROD, K C M G, M D 104 Illustrations 36s net

A Practical Guide to the Schick Test and Diphtheria and Scarlet Fever Immunisation By GUY BOUSFIELD, M B, B S (Lond) 4 Plates and 2 Text figures 5s net

Text=book of Differential Diagnosis of Internal Medicine By M MATTHES Translated from 4th German Edition by I W HELD, M D, and M H GROSS, M D 176 Illustrations 42s net

Pulmonary Tuberculosis : its Diagnosis, Prevention, and Treatment By W M CROFTON, M D 21 Illustrations 6s net

Therapeutic Immunisation : Theory and Practice. 7s 6d net
Chill : Its Dangers and Prevention. By MARIAN THORNETT, F R C S I With a Foreword by Dr JANE WALKER, CH Illustrated 3s 6d net

Studies in Influenza and its Pulmonary Complications By D BARTY KING, O B E, M D 7s 6d net

A Short Practice of Medicine. By R A FLEMING, M D, F R C P E, F R S E Third Edition 64 Illustrations 21s net

The Blood : how to Examine and Diagnose its Diseases By ALFRED C COLES, M D, D Sc, F R S E d m Third Edition 7 Coloured Plates 10s 6d net

Lectures on Medicine to Nurses. By HERBERT E. CUFF, M D, F R C S Seventh Edition 29 Illustrations 7s 6d net

On Alcoholism : Its Clinical Aspects and Treatment By FRANCIS HARE, M D 5s net

Recent Advances in Cardiology. By C F TERENCE EAST, M D, F R C P, and C W C BAIN, M C, M B Second Edition 10 Plates and 62 Text-figures 12s 6d net

Recent Advances in Study of Rheumatism. By F J POYNTON, M D, F R C P, Physician, Univ College Hospital, and B E SCHLESINGER, M R C P, M R C S, Physician, Children's Dept, Royal Northern Hospital 25 Illustrations 12s 6d net

Medicine

Massage

Recent Advances in Medicine Clinical—
Laboratory—Therapeutic By G E BEAUMONT D M FRCP and
 E C DOONS M B O M D BSc Sixth Edition 31 Illus 12s 6d net

Recent Advances in Allergy (Asthma, Hay-
fever, Eczema, Migraine, etc.) By G W BRAY M B BCh 99
 Illustrations 1s 6d net

Recent Advances in Pulmonary Tuberculosis
 By L S I BURRILL M D Second Edition 32 Plates and 17 Text
 figures 12s 6d net

Recent Advances in Chemotherapy By G M
 FINDLAY O B E M D D Sc 4 Plates and 11 Text figures 10s net

Massage its Principles and Practice By JAMES
 MENNELL M A M B B C Medical Officer Physico-Therapeutic Dept
 St Thomas's Hospital Third Edition *Ready July 1933*

ALSO BY J R MENNELL

Backache 48 Illustrations 10s 6d net

TRANSLATED AND EDITED BY DR MINA L DOBIE

Medical Gymnastics and Massage in General
 Practice By Dr J ARVEDSON Third Edition 8s 6d net

The Technique, Effects and Uses of Swedish
Medical Gymnastics and Massage By J
 ARVEDSON Second Edition 131 Illustrations 12s 6d net

Principles of Gymnastics for Women and Girls
 By ELLI HJORKSTEN Translated by VERA DAWSON BSc (Edin) and
 E M WILKIE 30 Illustrations 4s 6d net

Researches on Rheumatism By I J POYNION,
 M D FRCPLond and ALEXANDER PAINE M D BSLond With 106
 Illustrations and a Coloured Frontispiece 15s net

Physical Signs in the Chest and Abdomen By
 A J JEX BLAKE M D FRCP 27 Illustrations 9s 6d net

Ulcer of the Stomach and Duodenum By SAMUEL
 FENWICK M D FRCP and W SOLTAU FENWICK M D BSc 55 Illus-
 trations 10s 6d net **Cancer and other Tumours of the Stomach**
 70 Illustrations 10s 6d net

Uric Acid as a Factor in the Causation of
Disease By A HAIG M D FRCP Seventh Edition 75 Illustrations
 14s net **Uric Acid in the Clinic** 5s net **Uric Acid an Epitome**
of the Subject Second Edition 2s 6d net

Medical Hydrology By R FORTESCUE FOX M D 6s net

The Diabetic Life Its Control by Diet and
Insulin By R D LAWRENCE M D Physician in Charge of Diabetic
 Dept Kings College Hospital Seventh Edition 10 Illustrations
 8s 6d net

Physical Therapy in Diseases of the Eye, Ear,
Nose and Throat By A I HOLLENDER M D and M H COTILEY M D
 21s net

Medicine

Medicine : Essentials for Practitioners and Students By G E BEAUMONT, Physician, with Charge of Out patients, Middlesex Hospital 61 Illustrations 21s net

Medical Emergencies. By CHARLES NEWMAN, M D, M R C P, Junior Physician, King's College Hospital 8s 6d net

Taylor's Practice of Medicine. Fourteenth Edition Revised by Drs E P POULTON, C P SYMONDS, H W BARBER and R D GILLESPIE 64 Plates and 103 Figures 25s net

Clinical Atlas of Blood Diseases. By A PINEY, M D, and S WIARD, M D 2nd Edition 38 Illustrations, 34 in Colour 12s 6d net

ALSO BY DR A PINEY

Recent Advances in Hæmatology. Third Edition 4 Coloured Plates 18 Text figures 12s 6d net

Diseases of the Blood. Second Edition 65 Illustrations, 14 in Colour 18s net

Endocrine Diseases: Their Diagnosis and Treatment By W FALTA (Vienna) Translated by M K MEYERS, M D, with a Foreword by Sir A E GARROD, K C M G, M D 104 Illustrations 36s net

A Practical Guide to the Schick Test and Diphtheria and Scarlet Fever Immunisation By GUY BOUSFIELD, M B, B S (Lond) 4 Plates and 2 Text figures 5s net

Text-book of Differential Diagnosis of Internal Medicine By M MATTHES Translated from 4th German Edition by I W HELD, M D, and M H GROSS, M D 176 Illustrations 42s net

Pulmonary Tuberculosis: its Diagnosis, Prevention, and Treatment By W M CROFTON, M D 21 Illustrations 6s net **Therapeutic Immunisation: Theory and Practice.** 7s 6d net

Chill: Its Dangers and Prevention. By MARIAN THORNETT, F R C S I With a Foreword by Dr JANE WALKER, CH Illustrated 3s 6d net

Studies in Influenza and its Pulmonary Complications By D BARTY KING, O B E, M D 7s 6d net

A Short Practice of Medicine. By R A FLFMING, M D, F R C P E, F R S E Third Edition 64 Illustrations 21s net

The Blood: how to Examine and Diagnose its Diseases By ALFRED C COLES, M D, D Sc, F R S Edin Third Edition 7 Coloured Plates 10s 6d net

Lectures on Medicine to Nurses. By HERBERT E. CUFF, M D, F R C S Seventh Edition 29 Illustrations 7s 6d net

On Alcoholism: Its Clinical Aspects and Treatment By FRANCIS HARF, M D 5s net

Recent Advances in Cardiology. By C F TERENCE EAST, M D, F R C P, and C W C BAIN, M C, M B Second Edition 10 Plates and 62 Text-figures 12s 6d net

Recent Advances in Study of Rheumatism. By F J POYNTON, M D, F R C P, Physician, Univ College Hospital, and B E SCHLESINGER, M R C P, M R C S, Physician, Children's Dept, Royal Northern Hospital 25 Illustrations 12s 6d net

Medicine

Massage

Recent Advances in Medicine Clinical—
Laboratory—Therapeutic By G E BRAMMONT DM FRCP and
E C DODDS MIO MD BSc Sixth Edition 51 Illus 1s 6d net

**Recent Advances in Allergy (Asthma, Hay-
fever Eczema Milium etc)** By C W BEAT MB BCh 9S
Illustrations 1s 6d net

Recent Advances in Pulmonary Tuberculosis
By L S T BURRELL MD Second Edition 3s Plate and 17 Text
figures 12s 6d net

Recent Advances in Chemotherapy By G M
FINDLAY OBE MD DSc 4 Plates and 11 Text figure 10s net

Massage its Principles and Practice By JAMES
KENNELL MA MD BC Medical Officer Physio Therapeutic Dept
St Thomas's Hospital Third Edition *First July 1933*

ALSO BY DR KENNELL

Backache 48 Illustrations 10 6d net

TRANSLATED AND EDITED BY DR MINA L. LOEBE

Medical Gymnastics and Massage in General
Practice By Br J ARVEDSON Third Edition 8s 6d net

The Technique, Effects and Uses of Swedish
Medical Gymnastics and Massage By J
ARVEDSON Second Edition 131 Illustrations 12s 6d net

Principles of Gymnastics for Women and Girls
By ELLI HJORTSTEN Translated by A. E. DAWSON BS (Econ) and
E M WILKIE 30 Illustrations 8s 6d net

Researches on Rheumatism By F J POYNION
MD FRCP Lond and ALEXANDER PAINC MD BS Lond With 106
Illustrations and a Coloured Frontispiece 15s net

Physical Signs in the Chest and Abdomen By
A J JEN BLAKE MD FRCP 27 Illustrations 9s 6d net

Ulcer of the Stomach and Duodenum By SAMUEL
FENWICK MD FRCP and W SOLTAN FENWICK MD BS 50 Illu-
trations 10s 6d net **Cancer and other Tumours of the Stomach**
70 Illustrations 10s 6d net

Uric Acid as a Factor in the Causation of
Disease By A HARRIS MD FRCP Seventh Edition 7s Illustrations
14s net **Uric Acid in the Clinic** 3s net **Uric Acid an Epitome**
of the Subject Second Edition 4s 6d net

Medical Hydrology By R FORTESCUE FOX MD 6s net

The Diabetic Life Its Control by Diet and
Insulin By P D LAWRENCE MD Physician in Charge of Diabetic
Dept King's College Hospital Seventh Edition 10 Illustrations
8s 6d net

**Physical Therapy in Diseases of the Eye Ear,
Nose and Throat** By A P HOLLENDER MD and M H C TILLY MD
21s net

Surgery

Science and Practice of Surgery. By W. H. C. ROMANIS, F.R.C.S., and P. H. MITCHINER, F.R.C.S., Surgeons, St Thomas's Hospital. Fourth Edition. 2 vols. 752 Illustrations. Vol I, General Surgery. Vol II, Regional Surgery. 28s net.

BY THE SAME AUTHORS

Surgical Emergencies in General Practice. 158 Illustrations. 18s net.

Recent Advances in Radiology. By PETER KERLEY, M.D., B.Ch., D.M.R.E., Assistant Radiologist, Westminster Hospital, London. 120 Illustrations. 12s 6d net.

Radium Treatment of Cancer. By STANFORD CADE, F.R.C.S., Assistant Surgeon and Joint Lecturer on Surgery, Westminster Hospital. With 13 Coloured Plates and 49 Text-figures. 15s net.

Surgical Radiology. By A. P. BERTWISTLE, M.B., F.R.C.S. Edin. 21 Plates. 8s 6d net.

Surgery. Edited by G. E. GASK, C.M.G., D.S.O., F.R.C.S., and HAROLD W. WILSON, M.S., M.B., F.R.C.S., Surgeons, St Bartholomew's Hospital. With 39 Plates, 20 in colour, and 467 Text-figures. 30s net.

The After-Treatment of Wounds and Injuries. By R. C. ELMSLIE, M.S., F.R.C.S. 144 Illustrations. 15s net.

A Textbook of Surgery. By R. WARREN, M.D., F.R.C.S., With 504 Original Illustrations. 2 vols. 27s net.

Bowlby and Andrewes' Surgical Pathology and Morbid Anatomy. Revised by G. GIFFORD KEYS, M.D., F.R.C.S., Assistant Surgeon, St Bartholomew's Hospital. Eighth Edition. With 224 Illustrations. 21s net.

On Diseases of the Rectum and Anus, including the Sixth Edition of the Jacksonian Prize Essay on Cancer. By HARRISON CRIPPS, F.R.C.S. Fourth Edition. 14 Plates and 34 Illustrations. 10s 6d net.

Diseases of the Rectum, Anus, and Sigmoid Colon. By F. SWINFORD EDWARDS, F.R.C.S. Third Edition. 102 Illustrations. 10s 6d net.

Minor Surgery and Bandaging. Twentieth Edition. (Heath, Pollard and Davies.) By GWYNNE WILLIAMS, M.S., F.R.C.S., Surgeon, University College Hospital. 262 Engravings. 10s 6d net.

Surgical Nursing and After-Treatment. By H. C. RUTHERFORD DARLING, M.D., F.R.C.S., Surgeon, South Coast Hospital, Sydney. Fourth Edition. With 164 Illustrations. 8s 6d net.

Diseases of the Nose and Throat. By C. G. COAKLEY, M.D., F.A.C.S. Seventh Edition. 7 Colour Plates and 153 Figures. 18s net.

The Principles of Radiography. By J. A. CROWTHER, Sc.D., F.Inst.P. With 55 Illustrations. 7s 6d net.

Recent Advances in Radium. By W. ROY WARD, M.B., B.S., M.R.C.S., and A. J. DUDMAN SMITH, M.B., B.S., M.R.C.S., of The Radium Institute, London. 4 Coloured Plates and 110 black and white Illustrations. 21s net.

Surgery Anæsthetics Urinary Disorders

- A Text-book of Surgical Pathology** By C F W ILLINGWORTH MD FRCSE Late Clinical Tutor in Surgery Royal Infirmary Edinburgh and B M DICK FRCSE Late Clinical Tutor in Surgery Royal Infirmary Edinburgh 290 Illustrations 3s net
- The Operations of Surgery** Seventh Edition By P P LOWLANDS OIL MSc and FRCSE and PHILIP TURNER MS FRCSE Surgeons Guy's Hospital 2 vols 600 Illustrations 43 in Colour £1 10s net
- Recent Advances in Surgery** By W H OSWELL FRCSE Assistant Surgeon Guy's Hospital Second Edition 110 Illustrations 15s net
- Surgery in the Tropics** By SIR FRANK P CONNOR DSO FRCSE Professor of Surgery Bengal Medical College 99 Illustrations 1s 6d net
- Surgery in War** By A J HEIT FRCSE Lieut Col, F R C With 210 Illustrations 2s net
- Operative Surgery of the Head, Neck Thorax and Abdomen** By F H TAYLOR FRCSE With 300 Original Illustrations many in colour 3s net
- Synopsis of Surgery** By IVOR BACE FRCSE, Surgeon, St George's Hospital and A I EDWARDS FRCSE Assistant Surgeon Westminster Hospital 1s 6d net
- Synopsis of Surgical Diagnosis** By W H C POMANIS MB MC FRCSE 9s 6d net
- Synopsis of Surgical Pathology** By LEO PEARCE Gould MD FRCSE 6s net
- Inguinal Hernia, the Imperfectly Descended Testicle and Varicocele** By PHILIP TURNER MS FRCSE Assistant Surgeon Guy's Hospital With 22 Illustrations 10 6d net
- Practice and Problem in Abdominal Surgery** By ALFRED ERNEST MAYNARD MB BS and BS With 30 Illustrations 8s 6d net Abdominal Tuberculosis 2s Illustrations 1 6d net
- Surgical Emergencies** By PAUL SWAIN FRCSE Fifth Edition 149 Engravings 4s net
- Recent Advances in Anæsthesia and Analgesia** By C LANGTON HEWER MB BS Anæsthetist and Demonstrator of Anæsthetics St Bartholomew's Hospital 64 Illustrations 1s 6d net
- Chloroform a Manual for Students and Practitioners** By EDWARD LAWRIE MB Edin Illustrated 7s 6d net
- Stone in the Urinary Tract** By H P WINSBETH WHITE MB FRCSE 183 Illustrations 2s net
- Selected Papers on Stone, Prostate, and other Urinary Disorders** By I HARRISON FRCSE 12 Illustrations 3s net
- Diseases of the Kidney** By W CHUNG BAI, FRCSE and GEOFFREY EVANS MD FRCP 56 colour Plate and 100 Illustrations 31s net

Dermatology Neurology & Tropical Diseases

The Hair: Its Care, Diseases and Treatment.

By W J O'DONOVAN, OBE, MD, BS, Physician, Skin Department,
London Hospital 40 Illustrations 12s 6d net

A Text-Book of Diseases of the Skin. By J. H.

SEQUIRA, MD, FRCP, FRCS Fourth Edition 56 Plates in Colours
and 309 Text-figures 42s net

Skin—Its Uses in Six Phases By LEWIS E HERTSLET,

MRC S, L R C P With Forewords by Prof Sir LEONARD HILL, FRS,
and R P MACKENZIE, CMG, MB, CM, DPH 8 Plates 10s 6d net

Recent Advances in Neurology. By W RUSSELL

BRAIN, MD, Assistant Physician, London Hospital, and E B STRAUSS,
BM, BCh, Clinical Assistant to the Neurological and Psychiatric Clinic
of the University of Marburg Second Edition 39 Illustrations
12s 6d net

A Text-Book of Nervous Diseases. By W ALDREN

TURNER, MD, FRCP, and T GRAINGER STEWART, MB, MRC P
188 Illustrations 18s net

Paralysis and other Nervous Diseases in Child-

hood and Early Life By J TAYLOR, MD, FRCP 74 Illus-
trations 12s 6d net

Epilepsy and Other Chronic Convulsive Diseases,

their Causes, Symptoms and Treatment. By Sir W R GOWERS,
MD, FRS Second Edition 10s 6d net

Malarial Nephritis. By G GIGLIOLI, MD (Italy), DTM

&H (Eng) 17 Illustrations 8s 6d net

Public Health Practice in the Tropics. By J.

BALFOUR KIRK, MB, DPH, DTM &H 80 Illustrations 15s net

The Malarial Fevers of British Malaya. By

HAMILTON WRIGHT, MD Map and Charts 3s net **The Etiology
and Pathology of Beri-Beri.** With Map and Charts 3s net

The Nematode Parasites of Vertebrates. By

WARRINGTON YORKE, MD, and P A MAPLESTONE, MB, DSO Fore-
word by C W STILES 307 Illustrations 36s net

Recent Advances in Tropical Medicine. By Sir

LEONARD ROGERS, CIE, MD, FRS, FRCS, FRCP Second Edition
16 Illustrations 12s 6d net

Malay Poisons and Charm Cures. By J D

GIMLETTE, MRC S, L R C P Third Edition 3 Plates 10s 6d net

Tropical Medicine. By Sir LEONARD ROGERS, CIE, MD,

FRCP, FRCS, FRS, and General JOHN W D MEGAW, CIE,
MB, BCh 1 Coloured Plate 77 Illustrations 14s net

The Health Game. A Popular Guide for the Tropics

By B E WASHBURN, MD 20 Illustrations 5s net

Midwifery

Gynæcology

The Queen Charlotte's Practice of Obstetrics

By J B BANISTER MD FRC S A W BOURNE M F FCS T B DAVIES MD FPCS I G PHILLIPS MS FPCS L C LIVETT MC FPCS C S LANE ROBERTS MS FICS Members of the Staff of the Hospital Second Edition 74 Illustration 4 Coloured Plate 1s net

Recent Advances in Obstetrics and Gynæcology

By ALECK W BOURNE FPCS and L LIE WILLIAMS FICS Of the Staff of the Hospital St Mary's Hospital 3rd Edition 47 Illustrations 1s 6d net

The Difficulties and Emergencies of Obstetric

Practice By COMUS BERKELEY MD FPCS and VICTOR BONNEY MD FRC S Third Edition With 309 Original Illustration 3s net

Manual of Midwifery

By I W LOEN, MD, C Midwifery, FRC P Lond and EARDLEY HOLAND MD FRC P FPCS Seventh Edition 9 Plates and 389 Illustration 1s net

Gynæcology

By T W FORD and C LOCKYER MD FRC P FPCS Third Edition 56 Illustrations and 2 Coloured Plates 3s net

Practical Midwifery

By GIBSON FITZGIBSON MD, FRCPI With 175 Illustrations 16s net

By HENRY JELLETT MD FRCPI EX MASTER ROTUNDA HOSPITAL DUBLIN

A Short Practice of Midwifery, embodying the

Treatment adopted in the Rotunda Hospital Dublin Ninth Edition 3 Coloured Plates and 283 Illustrations 1s net

A Short Practice of Midwifery for Nurses, with

a Glossary of Medical Terms and the Regulations of the CMB Ninth Edition 7 Plates and 183 Text Illustrations 6d net

The Causes and Prevention of Maternal

Mortality 1s net

A Practice of Gynæcology

Fifth Edition 15 Coloured Plates 417 Illustrations (many coloured) 2s net

A Short Practice of Gynæcology

Revised by PIERRE P TOTTENHAM MD FRCPI With 315 Illustrations (many in colour) Sixth Edition 1s net

Handbook of Midwifery

By R I TOTTENHAM MD FRCPI Professor of Obstetrics and Gynæcology University of Hong Kong 10 Illustrations 10s 6d net

A Manual for Midwives

By J B BANISTER MD FPCS Fourth Edition 33 Illustration 6s net

Cæsarean Section

By I PANCES IVENS KN WELCH (B F M B MS Honorary Surgeon Clapham Maternity Hospital and Lecturer

A Clinical Manual of the Malformations and

Congenital Diseases of the Fœtus By Prof Dr F BERNHARDT Translated and Annotated by G BLACKER MD FPCS 16 Illustrations

Practical Talks to Midwives

By E M DUFFELL SPN Sister Tutor Post Certificate School for Midwives Cambridge 17 Illustrations 3s 6d net

By R A GIBBONS MD FRC S

A Lecture on Oysmenorrhœa

1s 6d net A Lecture on Sterility its Etiology and Treatment 1s 6d net A Lecture on Pruritus Vulvæ its Etiology and Treatment 1s 6d net

Medical Jurisprudence Ophthalmology

An Introduction to Forensic Psychiatry in the Criminal Courts By W NORWOOD EAST, M D 16s net

Some Famous Medical Trials. By L A PARRY, M D, F R C S 10s 6d net

Forensic Medicine. A Text-book for Students and Practitioners By SYDNEY SMITH, M D, D P H, Regius Professor of Forensic Medicine, Univ of Edin Third Edition 170 Illustrations 24s net

Recent Advances in Forensic Medicine. By SYDNEY SMITH, M D, D P H, and J GLAISIER, M D, Ch B, Regius Professor of Forensic Medicine, University of Glasgow 66 Illustrations 12s 6d net

Forensic Medicine. Illustrated by Photographs and Descriptive Cases By H LITTLEJOHN, F R C S Ed 183 Illus 15s net

Medical Jurisprudence: its Principles and Practice By A S TAYLOR, M D, F R C P, F R S Eighth Edition, by SYDNEY SMITH, M D, D P H, and W G H COOK, LL D, M Sc, Barrister at Law 2 vols £3 3s net

Recent Advances in Ophthalmology. By W. STEWART DUKF-ELDER, M D, F R C S Second Edition 4 Coloured Plates and 110 Text-figures 12s 6d net The Practice of Refraction. 208 Text-figures 12s 6d net

A Handbook of Ophthalmology By HUMPHREY NEAVE, F R C S, and F A WILLIAMSON-NOBLE, F R C S 12 Coloured Plates 194 Illustrations 12s 6d net

Medical Ophthalmology. By R FOSTER MOORE, O B E, F R C S Second Edition 92 Illustrations 18s net

Refraction of the Eye. By G HARTRIDGE, F R C S 16th Edition 110 Illustrations, 7s 6d net **The Ophthalmoscope: a Manual for Students.** 6th Edition 65 Illustrations and 4 Plates 6s 6d net

Diseases of the Eye: a Manual for Students and Practitioners By SIR J H PARSONS, D Sc, F R C S, F R S, Ophthalmic Surgeon, University College Hospital Sixth Edition 318 Illustrations and 19 Coloured Plates 18s net **Elementary Ophthalmic Optics, including Ophthalmoscopy and Retinoscopy.** 66 Illustrations 6s 6d net

The Principles of Ophthalmoscopy and Skiascopy By G F ALEXANDER, M B, C M 31 Illustrations 5s net

The Ophthalmoscope and How to Use It. By A FREELAND FERGUS, LL D, M D Second Edition 17 Illustrations 3s 6d net

Refraction of the Eye, including Elementary Ophthalmic Optics. By CHARLES GOULDEN, O B E, M D, F R C S 180 Illustrations 10s 6d net

Sight Testing made Easy. By W W HARDWICKE, M D, M R C P Fourth Edition 12 Engravings 5s net

The Slit-Lamp Microscopy of the Living Eye. By F KOBY Translated by CHARLES GOULDEN, O B E, M D, F R C S, and CLARA L HARRIS, M B, Ch B Second Edition 104 Illus 15s net

Ophthalmic Nursing. By M H WHITING, O B E, F R C S 51 Illustrations 5s net

Ophthalmological Society of the United Kingdom Transactions Annually 30s net

Otology & Pædiatrics & Dentistry

The Labyrinth of Animals, including Mammals,

Birds, Reptile and Amphibian. By ALBERT A. GRAY M.D. (Glas)
F.P.S.E. Vol I with 31 Stereoscopic Plates 1s net (including Stereo
scope) Vol II with 40 Stereoscopic Plates 2s net

The Pharmacopœia of the Hospital for Diseases

of the Throat, Nose and Ear. Seventh Edition 2s 6d net

Mothercraft: Antenatal and Postnatal

By I. C. JEWELLERY D.M. F.I.C.P. Physician in Charge of the Children
Dept. St. Thomas's Hospital. 11 Illus. 1s in Colour 10s 6d net

The Mothercraft Manual

By M. J. DIDIARD S.R.N.,
Matron Mothercraft Training Society. 5th Edition. 31 Illus. 3s 6d net

Recent Advances in Diseases of Children

By W. J. HARRISON D.S.O. D.M. F.I.C.P. and W. G. WILLIS M.D.
M.F.C.P. Second Edition. 20 Plates and 31 Text figures. 15s net

The Modern Practice of Pediatrics

By WILLIAM
PALMER LUCAS M.D. LL.D. 126 Illustrations. 30s net

Premature and Congenitally Diseased Infants

By JULIUS H. HES. M.D. With 169 Illustrations. 1s net

The Diseases of Children

By the late Sir J. F.
GOODHART Bart. Edited by C. F. STILL M.D. F.I.C.P. 12th Edition
64 Illustrations. 2s net

The Wasting Diseases of Infants and Children

By EUSTACE SMITH M.D. F.I.C.P. Sixth Edition. 6s net

An Introduction to Dental Anatomy and Phy-

siology Descriptive and Applied. By A. HOPKINSON SMITH L.D.S. Eng.
With 61 Plates and 1340 Illustrations. 1s net. The Normal and Patho-
logical Histology of the Mouth. Vol I Normal Histology. Vol II
Pathological Histology. With 658 Illustrations. 2 vol. £. 2s 6d per set

Dental Anatomy, Human and Comparative

By CHARLES S. JONES M.A. F.F.S. Eighth Edition. Edited by H. W.
MAESTER TINKER M.D. I.L.S. with assistance of C. BOWLER HENRY
L.R.C.P. M.R.C.S. L.D.S. (Eng.) 325 Illustrations. 1s net

A System of Dental Surgery

By Sir JOHN JONES,
F.R.S. Revised by C. S. JONES M.A. F.R.S. and WALTER S. NOWELL
M.A. Oxon. Fifth Edition. 318 Engravings. 15s net

An Atlas of Dental Extractions, with Notes on

the Causes and Relief of Dental Pain. By C. EDWARD WALLIS M.P.C.S.
L.D.S. Second Edition. With 11 Plates. 6s net

A Manual of Dental Metallurgy

By ERNEST A.
SMITH Assay Office Sheffield. Fourth Edition. 37 Illustrations. 12s 6d net

Synopsis of Dentistry

By A. B. G. UNDERWOOD M.B.
B.S. L.D.S. Eng. With 10 Illustrations. 9s 6d net

Handbook of Mechanical Dentistry

By J. L.
DUDLEY BUXTON L.D.S. Dental Surgeon University College Hospital
With 168 Illustrations. 12s 6d net

Operative Dentistry

By W. H. O. MCGHEE M.D.
D.D.S. 1040 Illustrations. 4s net

Chemistry

Colloid Aspects of Food Chemistry and Technology. By W CLAYTON,
D Sc, F I C 64 Illustrations 36s net

A Chemical Dictionary. By Ingo W D HACKH 232 Illus 45s net

The Chemical Analysis of Foods. By H E COX, M Sc, Ph D, F I C,
Public Analyst for Borough of Hampstead 39 Illustrations 18s net

Recent Advances in Analytical Chemistry. Edited by C A MITCHELL,
D Sc Vol I—Organic 6 Plates and 19 Text figures 15s net Vol II—Inorganic
26 Illustrations 15s net

Parry's Cyclopædia of Perfumery. By E J PARRY, B Sc, F I C, F C S,
Analytical and Consulting Chemist 2 Vols 36s net

Gasworks Laboratory Handbook. By W I INESON, Chief Chemist,
Bradford Corporation Gasworks 55 Illustrations 9s 6d net

Inorganic and Organic Chemistry. By C L BLOXAM Eleventh Edition
By A G BLOXAM, F I C, and S JUDD LEWIS, D Sc, F I C 310 Illustrations 36s net

A Text-Book of Practical Chemistry. By G F HOOD, M A, B Sc,
and J A CARPENTER, M A With 162 Illustrations Price 21s net

Explosives. Their Manufacture, Properties, Tests, and History. By
ARTHUR MARSHALL, A C G I, F I C, F C S Second Edition 3 vols With 172 Illustrations
Vols I and II, £23s net Vol III, £22s net A Short Account of Explosives
7s 6d net A Dictionary of Explosives 15s net

Introduction to Qualitative Chemical Analysis. By C R FRESENIUS
Seventh Edition, translated by C A MITCHELL, M A 57 Illustrations 36s net

Treatise on Applied Analytical Chemistry. Edited by Prof V VILLAR-
ECCHIA Translated by T H PORR, B Sc Vol I With 58 Illustrations 21s net
Vol II With 105 Illustrations 25s net

Treatise on General and Industrial Chemistry. By Dr ETTORE MOLINARI
Second English Edition Translated by T H PORR, B Sc, F I C Vol I—Inorganic
With 328 Illustrations and 2 Plates 42s net Vol II—Organic Pt I 254 Illustrations
30s net Pt II 303 Illustrations 30s net

Elementary Analytical Chemistry, Qualitative and Quantitative By
F CLOWE, and J B COLEMAN Eleventh Edition Revised by F ARNALL, Ph D, and F N
APPLEYARD, B Sc 6s net

Organic Medicaments and their Preparation. By M FOURNEAU
Translated by W A SILVERSLER, M Sc 22 Illustrations 15s net

The Plant Alkaloids By T A HENRY, D Sc 2nd Edition 8 Plates 26s net

Industrial Organic Analysis. By PAUL S ARUP, B Sc, A C G I Second
Edition 25 Illustrations 12s 6d net

An Elementary Text-Book of General Microbiology. By WARD GILTNER,
Prof of Bact and Hygiene, Michigan State Coll 99 Illus 15s net

Microbiology for Agricultural and Domestic Science Students. Edited
by C E MARSHALL Third Edition With 186 Illustrations 24s net

Cocoa and Chocolate their Chemistry and Manufacture. By R
WHYMPER Second Edition With 16 Plates and 10 Figures 42s net

Reagents and Reactions. By E TOGNOLI Trans by C A MITCHELL 7s 6d net

Colloid Chemistry of the Proteins. By Prof Dr W PAULI Translated
by P C L THORPE, M A With 27 Diagrams 8s 6d net

The Formation of Colloids. By THE SVEDBERG 22 Illustrations 7s 6d net

Laboratory Manual of Elementary Colloid Chemistry. By E HATSCHER
Second Edition With 21 Illustrations 7s 6d net

Practical Physiological Chemistry. By P B HAWK, M S, Ph D Tenth
Edition 6 Coloured Plates and 280 Text figures 32s net

The Atmospheric Nitrogen Industry. By Dr I B WAESER Translated
by E FALSMAN, Ph D 2 Vols 72 Illustrations 42s net

Recent Advances in Physical Chemistry. By S GLASSTONE, D Sc, Ph D,
F I C 32 Illustrations 15s net

Chemistry

- Adulteration and Analysis of Foods and Drugs** By J F LIVERSIDGE
FIC Ph C Formerly Public Analyst to the City of Birmingham. Forwards by the
Right Honourable Viscountess CHAMBERS M P Formerly Master of Health 6 net
- Modern Methods of Cocoa and Chocolate Manufacture** By H W
BRW & D Co 103 Illustrations 1 net
- Catalysis and its Industrial Applications** By E B MAXTER D Sc Ph D
FIC Title and 60 Illustrations 70 net
- The Preparation and Analysis of Organic Compounds** By J BERNARD
Co M & A B C Sc FIC and FANCIS ARNOLD Ph D M Sc 4 Illustrations 13s net
- Theoretical Organic Chemistry** By F ARNOLD Ph D M Sc and F W
HOBBS M Sc Part I 30 Ill 115 Experiments 10 6d net Part II 12 6d net
- The Chemistry of the Proteins and its Economic Applications** By
DOUGLAS JOSEPH LLOYD D Sc FIC 50 Illustrations 10 6d net
- A Systematic Handbook of Volumetric Analysis** By F SUTTON 11th
Edition by W L SUTTON FIC and A L JOHNSON FIC 170 Illustrations 3 net
- Quantitative Organic Microanalysis** By F PEROL Translated by
E FRYAN & Ph D FIC Second Edition 51 Illustrations 15 net
- The Fundamental Processes of Dye Chemistry** By H E PIERCE DAVID
Translated by F A MASON Ph D With Illustrations and 49 Plates Price 1 net
- A Junior Inorganic Chemistry** By P H SPEAR M A Second Edition
With 9 Illustrations 6 6d net Also Part I (plus Atomic Theory) 3 6d net
- Ammonia and the Nitrides** With Special Reference to their Synthesis
By E B MAXTER Ph D M Sc 6d net
- The Analyst's Laboratory Companion** By A E JOHNSON B Sc FIC
Fifth Edition 10 6d net
- Allen's Commercial Organic Analysis a Treatise on the Properties
Methods of Analysing Proximate Analytical Examination etc of Organic Chemical and
Ferments. Fifth Edition in 10 vols Edited by C A MERRILL M A D Sc FIC B Sc
9 Vols 8 SB and E C L N O A B Ph D Vols 1 & 2 ready 3 net each volume**
- Volumetric Analysis for Students of Pharmaceutical and General
Chemistry** By C H H W M B Sc FIC Fourth Edition 6d net
- Quantitative Chemical Analysis (Clowes & Coleman)** Thirteenth Edition
Revised by D Stoddart Ph D AIC & J D R B Sc AIC 133 Illustrations
10 1s net
- Qualitative Analysis** By F CLOWES D Sc and J B COLEMAN A P C Sc
Ninth Edition 51 Illustrations 1 6d net Elementary Practical Chemistry Part
I General Chemistry 50th Edition 6 Illustrations 6 net
- Researches on the Affinities of the Elements** By G MARTIN 16s net
- Oils Fats and Fatty Foods** By E P BOLTON FIC 2nd Edition 113s net
- The Chemistry Flavouring and Manufacture of Chocolate Confectionery
and Cocoa** By H P JONES M Sc FIC Illustrated 2s 6d
- Laboratory Manual for the Detection of Poisons and Powerful Drugs**
By D W AUSTIN Translated by W H W 3rd Edition 60 Illustrations 3 net
- TEXT BOOKS OF CHEMICAL RESEARCH AND ENGINEERING**
Edited by W P DREAPER OBE FIC
- Clouds and Smokes** The Properties of Disperse Systems in Gases
By W E GORDON D Sc 30 Illustrations 10 6d net
- The Theory of Emulsions and their Technical Treatment** By W
CLARKE D Sc 8th Edition With 4 Illustrations 15 net
- Catalytic Hydrogenation and Reduction** By E B MAXTER Ph D
B Sc FIC With 1 Illustration 5 net
- Molecular Physics and the Electrical Theory of Matter** By J A
COWAN M A Sc D Phil Fourth Edition With 33 Illustrations 6d net
- Notes on Chemical Research** By W P DREAPER OBE FIC
Second Edition 6d net
- An Introduction to the Physics and Chemistry of Colloids** By
EMIL HAUSER Fifth Edition With 4 Illustrations 6d net
- Catalysis and its Industrial Applications** By E JOBLING A P C Sc
B Sc FIC Second Edition With 1 Illustrations 6d net

Physics

Botany

Miscellaneous

Recent Advances in Atomic Physics. By GAETANO CASTELFRANCHI, Professor in the High School for Engineers, Milan
Translated by W S STILES, Ph D, and J W T WALSH, M A, D Sc, of
The National Physical Laboratory, Teddington 2 Vols 190 Illustrations
15s net each vol

Recent Advances in Physics (Non-Atomic). By F H NEWMAN, D Sc 51 Illustrations 15s net

Elementary Physics. By G STEAD, M A Cantab, Univ. Lect in Physics, Cambridge Fourth Edition 294 Illustrations 10s 6d net

The Physics of X-Ray Therapy. By W V. MAYNEORD, M Sc, Physicist, Cancer Hospital 106 Illus 10s 6d net

A Text-book of Physics. Edited by A W DUFF, D Sc, Seventh Edition 630 Illustrations 18s net

Recent Advances in Microscopy. Edited by A PINEY, M D, M R C P, Director, Pathological Department, Cancer Hospital, London 83 Illustrations 12s 6d net

Recent Advances in Town Planning. By THOMAS ADAMS, P P T P I, F S I, with F LONGSTRECH THOMPSON, V P T P I, F S I, E MAXWELL FRX, B Arch, A R I B A, and J W R ADAMS, A M T P I 2 Col Maps and 87 Illustrations 25s net

The Microtome's Vade-Mecum. By ARTHUR BOLLES LEF Ninth Edition Edited by J BRONTÉ GATENDY, D Sc 30s net

Recent Advances in Plant Physiology. By E BARTON-WRIGHT, M Sc Second Edition 51 Illustrations 12s 6d net
Recent Advances in Botany. 60 Illus 12s 6d net

A Text-book of Botany, for Medical and Pharmaceutical Students By J SMALL, D Sc, F L S Second Edition 1350 Illustrations 21s net
Practical Botany. 35 Illustrations 10s 6d net
Pocket Lens Plant Lore 25 Illustrations 5s net

Elementary Histological Technique for Animal and Plant Tissues By J T HOLDER, F R M S 23 Illus 7s 6d net

Plant Anatomy. By W C STEVENS, Professor of Botany in the University of Kansas Fourth Edition 155 Illustrations 21s net

A Text-book of Mycology and Plant Pathology. By J W HARSHBERGER With 271 Illustrations 24s net

Recent Advances in Entomology. By A D IMMS, D Sc, F R S 84 Illustrations 12s 6d net

Recent Advances in Plant Genetics. By F. W SANSOME, Ph D, F L S, F R S E, and J PHILIP, B Sc, F L S, Research Workers, John Innes Horticultural Institution 55 Illus 15s net

Recent Advances in Cytology. By C D DARLINGTON, D Sc, Ph D, Cytologist, John Innes Horticultural Institution Foreword by J B S HALDANE, M A, F R S 8 Plates, 109 Text-figures and 66 Tables 18s net

Recent Advances in Agricultural Plant Breeding. By H HUNTER, Hon M A (Cantab), D Sc (Leeds), and H MARTIN LEAKE, M A, Sc D (Cantab), with a Foreword by SIR ROWLAND H BIFFEN, M A, F R S 16 Plates 15s net

J. & A. CHURCHILL

LONDON: 40, GLOUCESTER PLACE, PORTMAN SQUARE, W. 1

